

Fig. 1

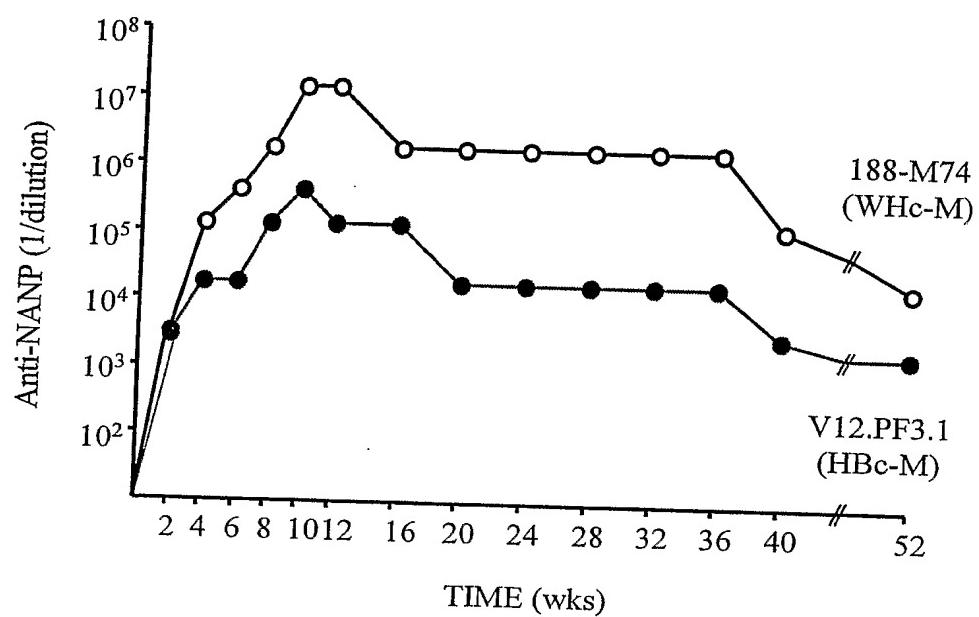
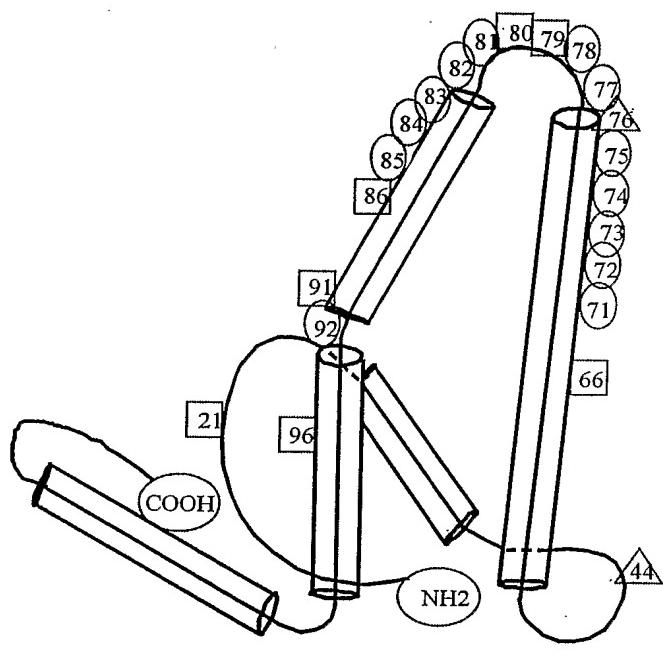


Fig. 2



○ tolerant
△ intermediate
□ intolerant

Fig. 3

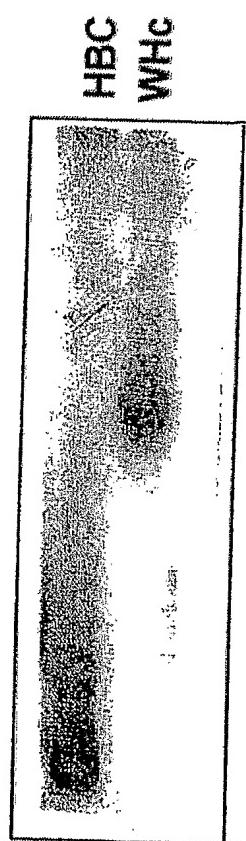


Fig. 4

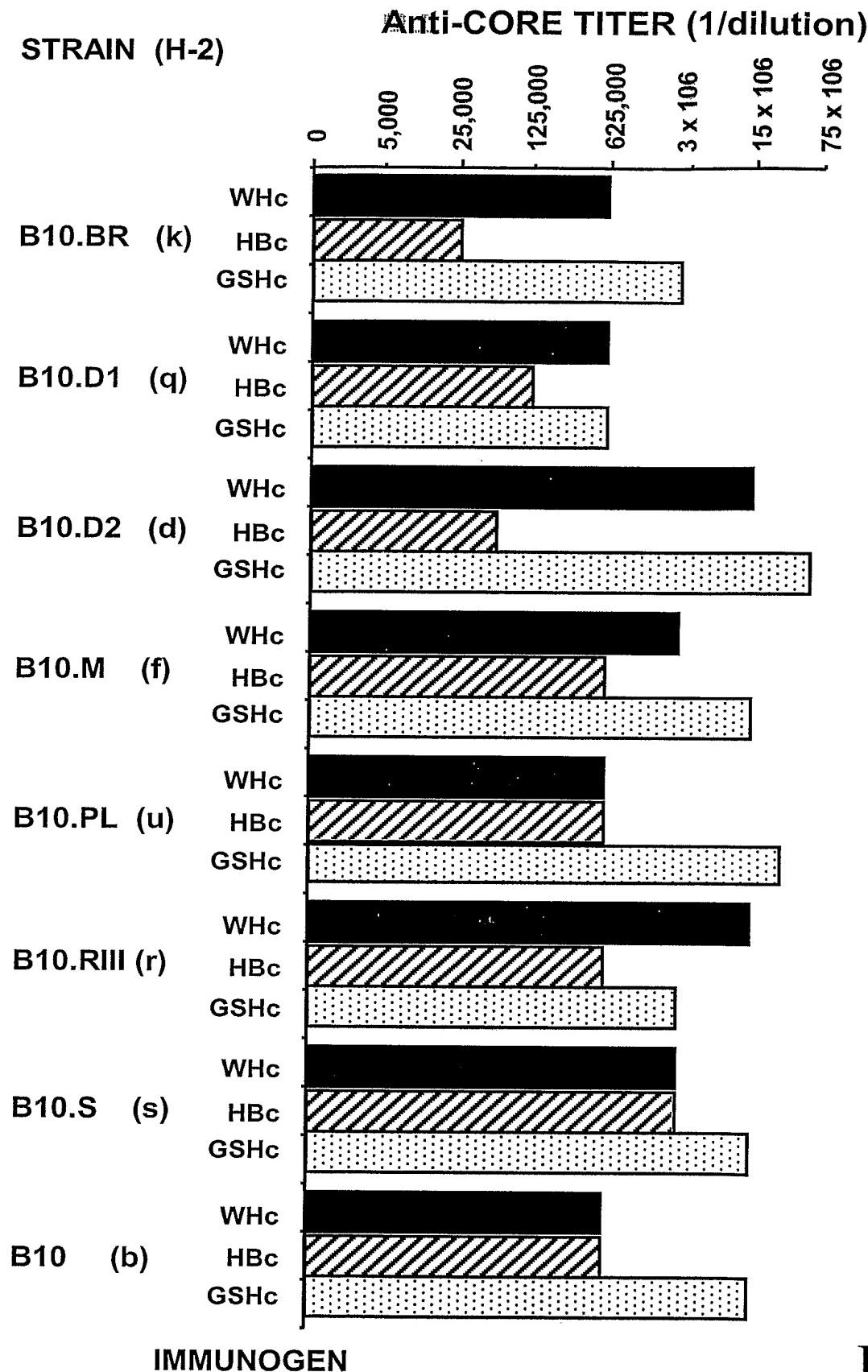


Fig. 5

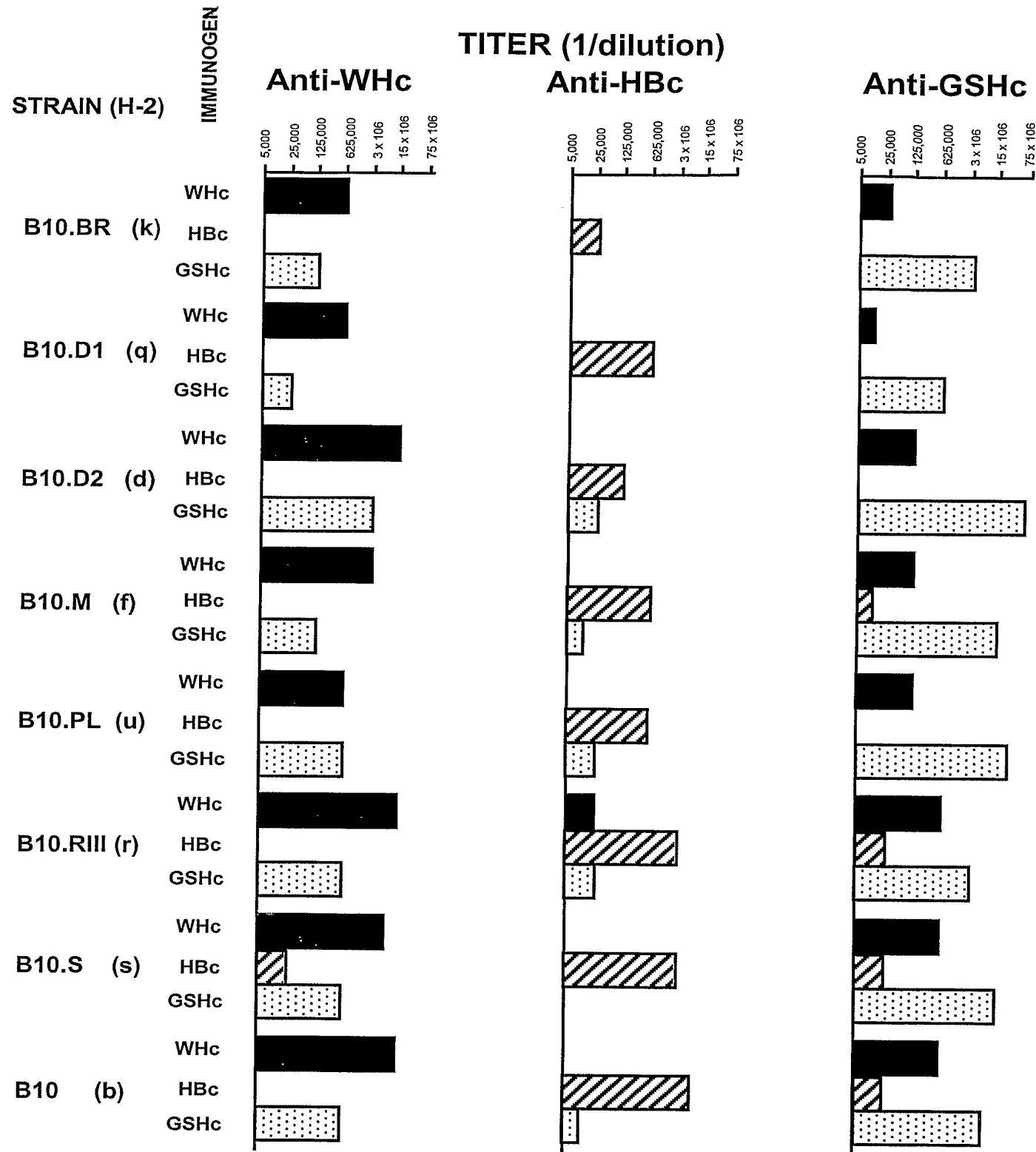


Fig. 6

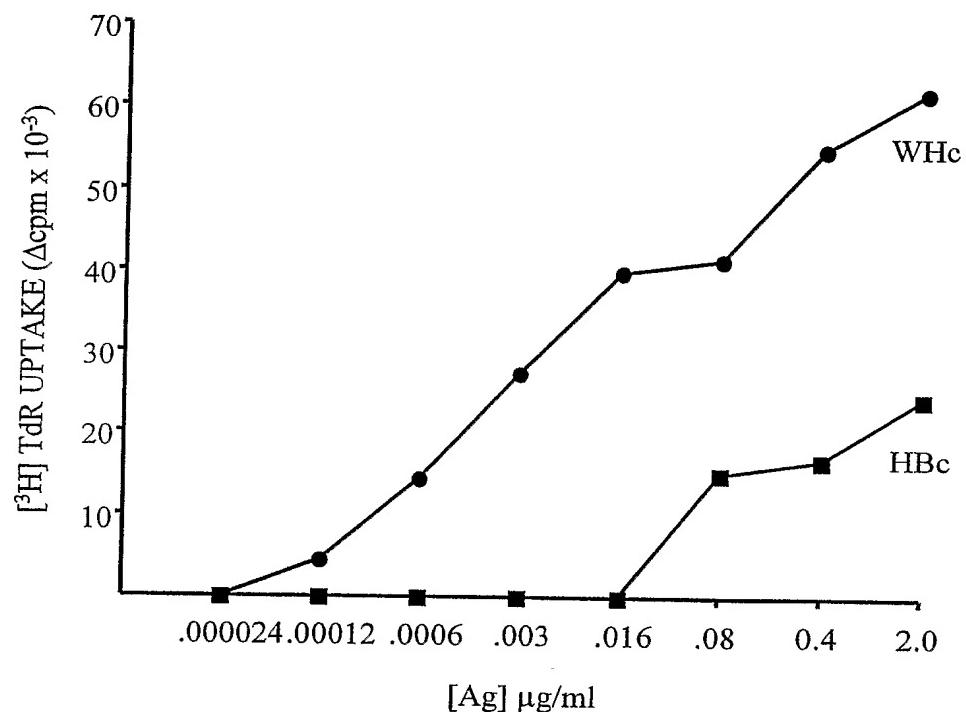
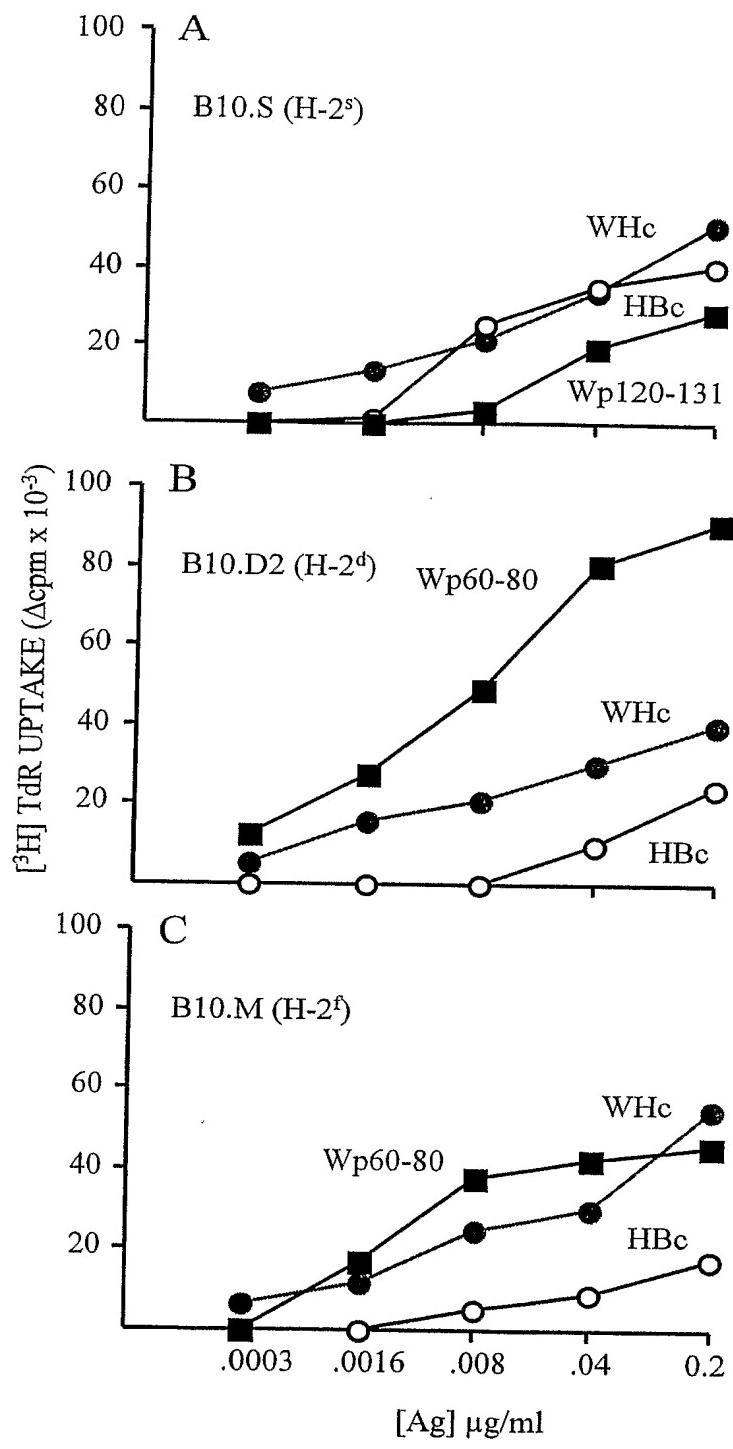


Fig. 7

**Fig. 8**

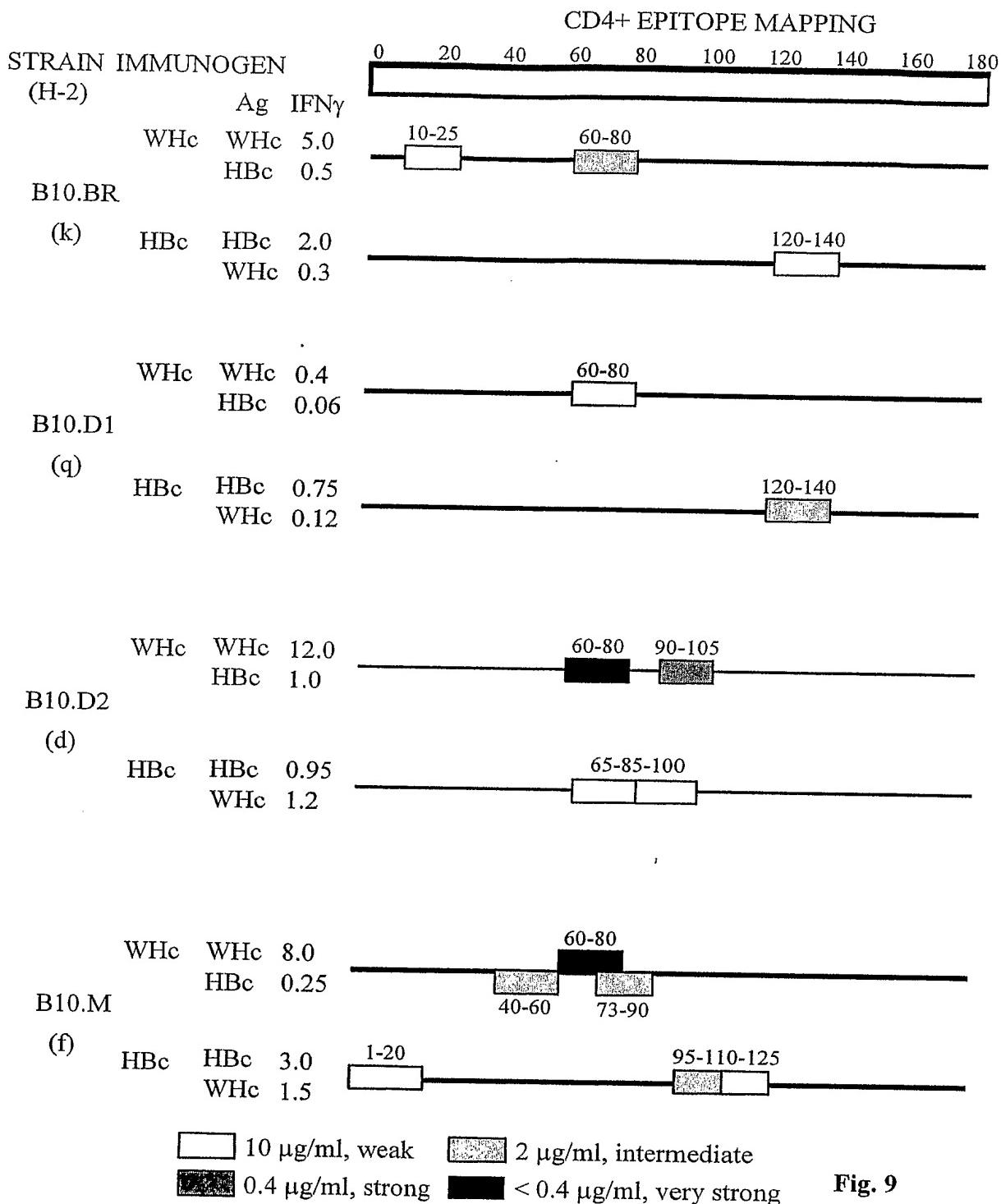
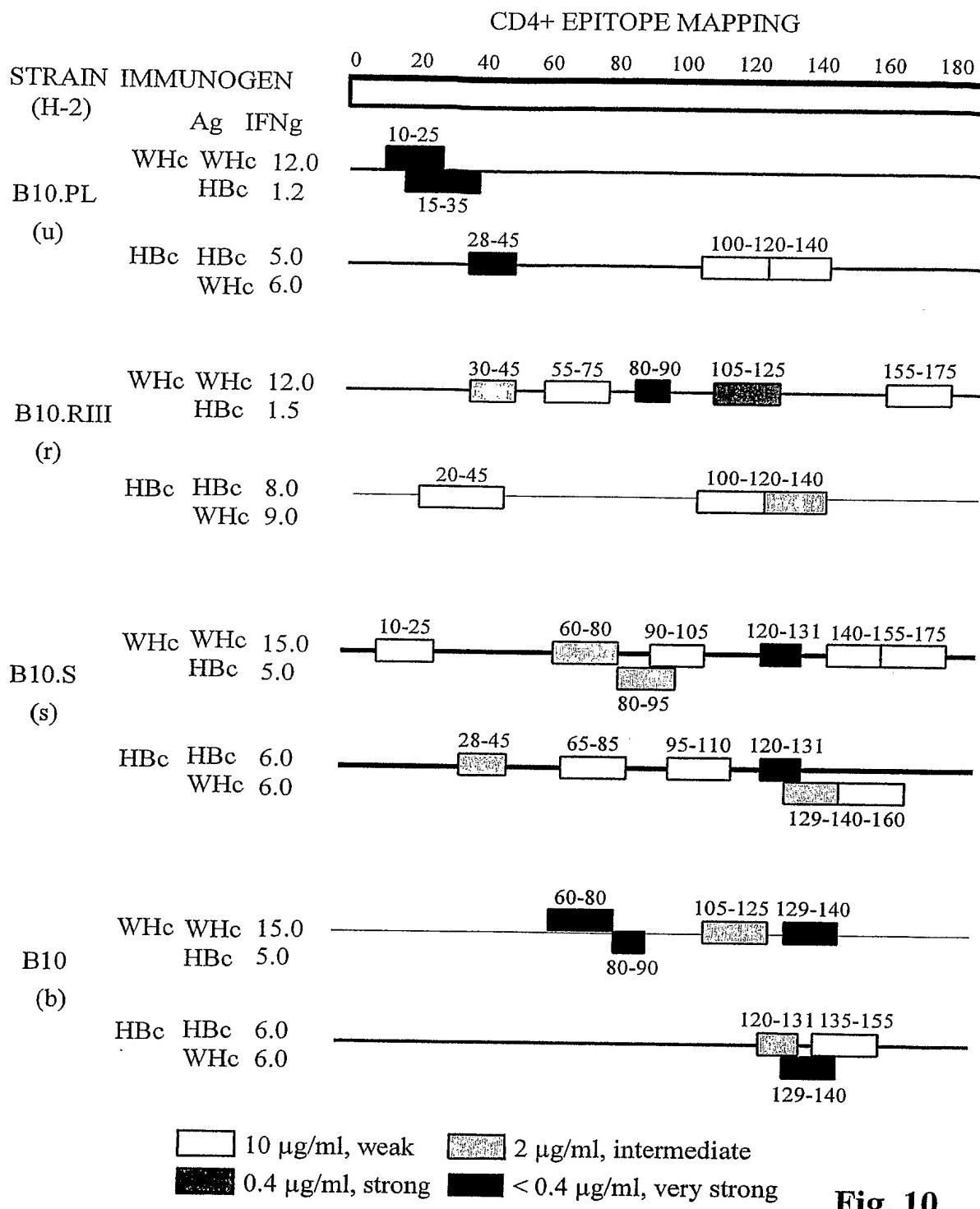
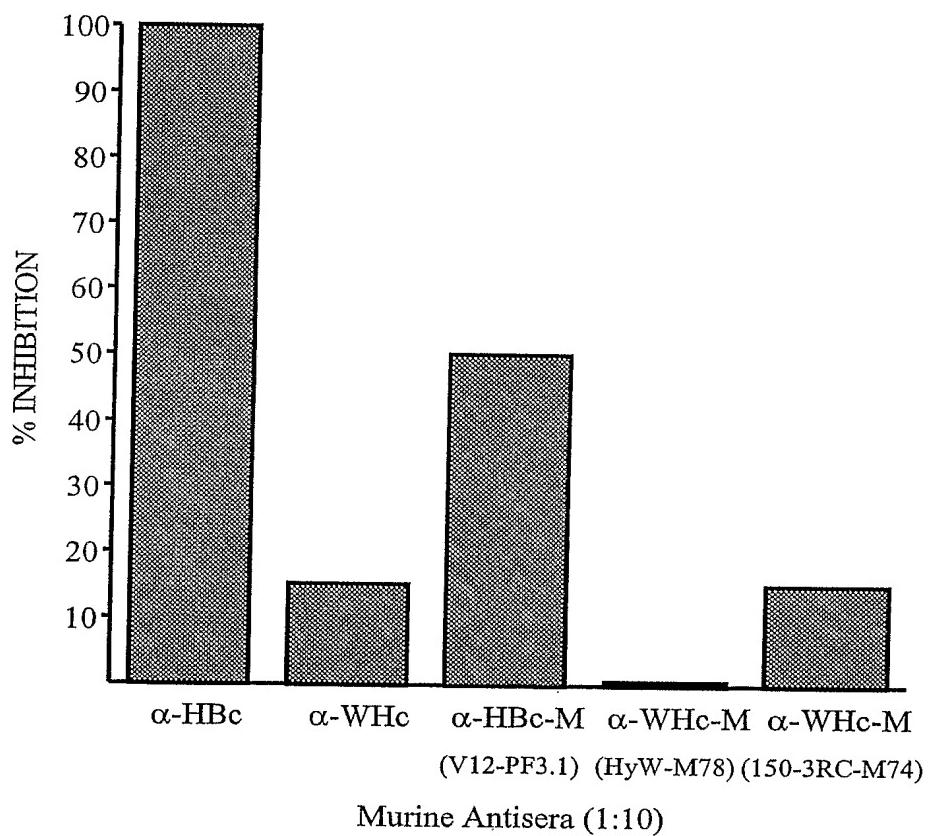
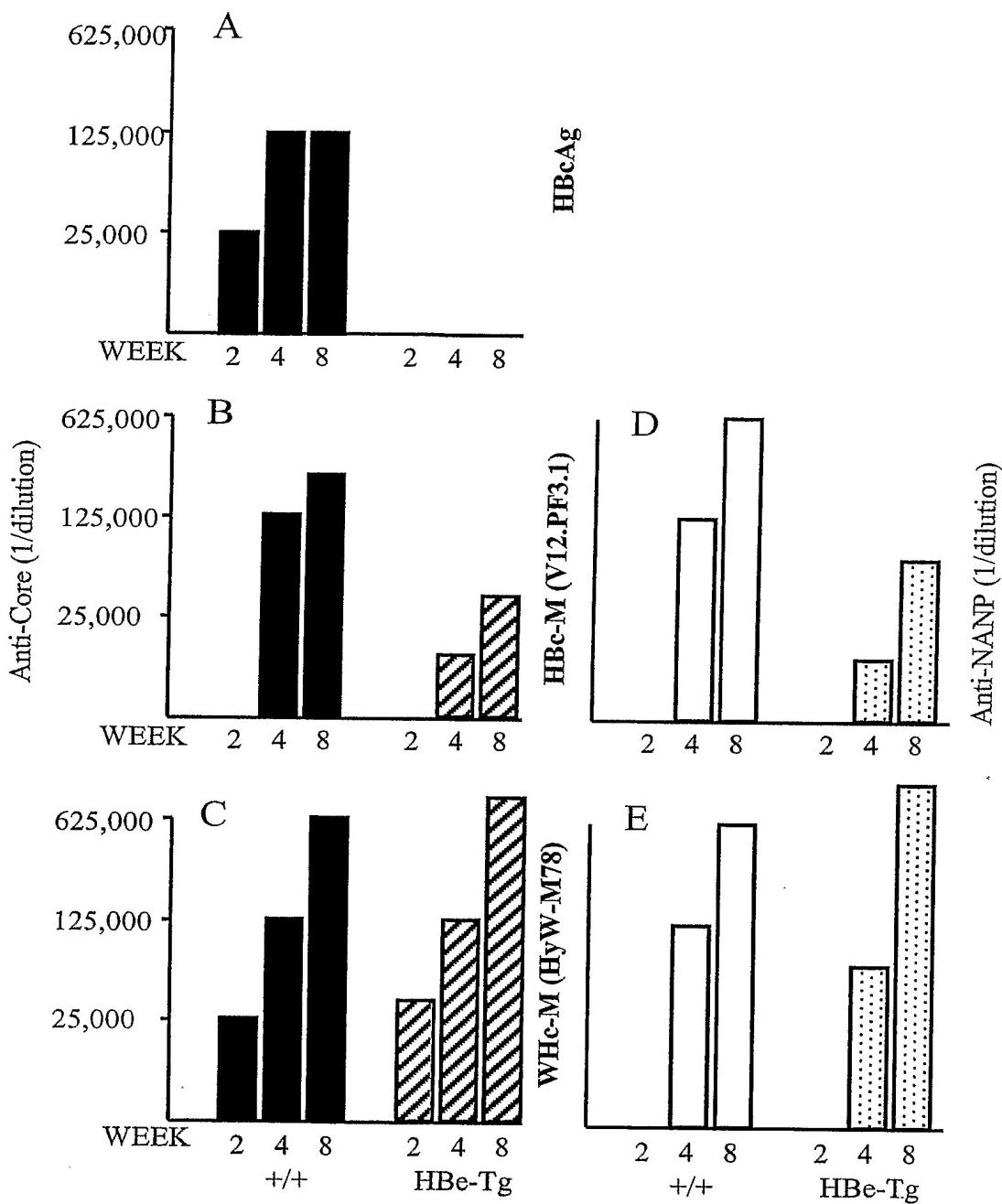
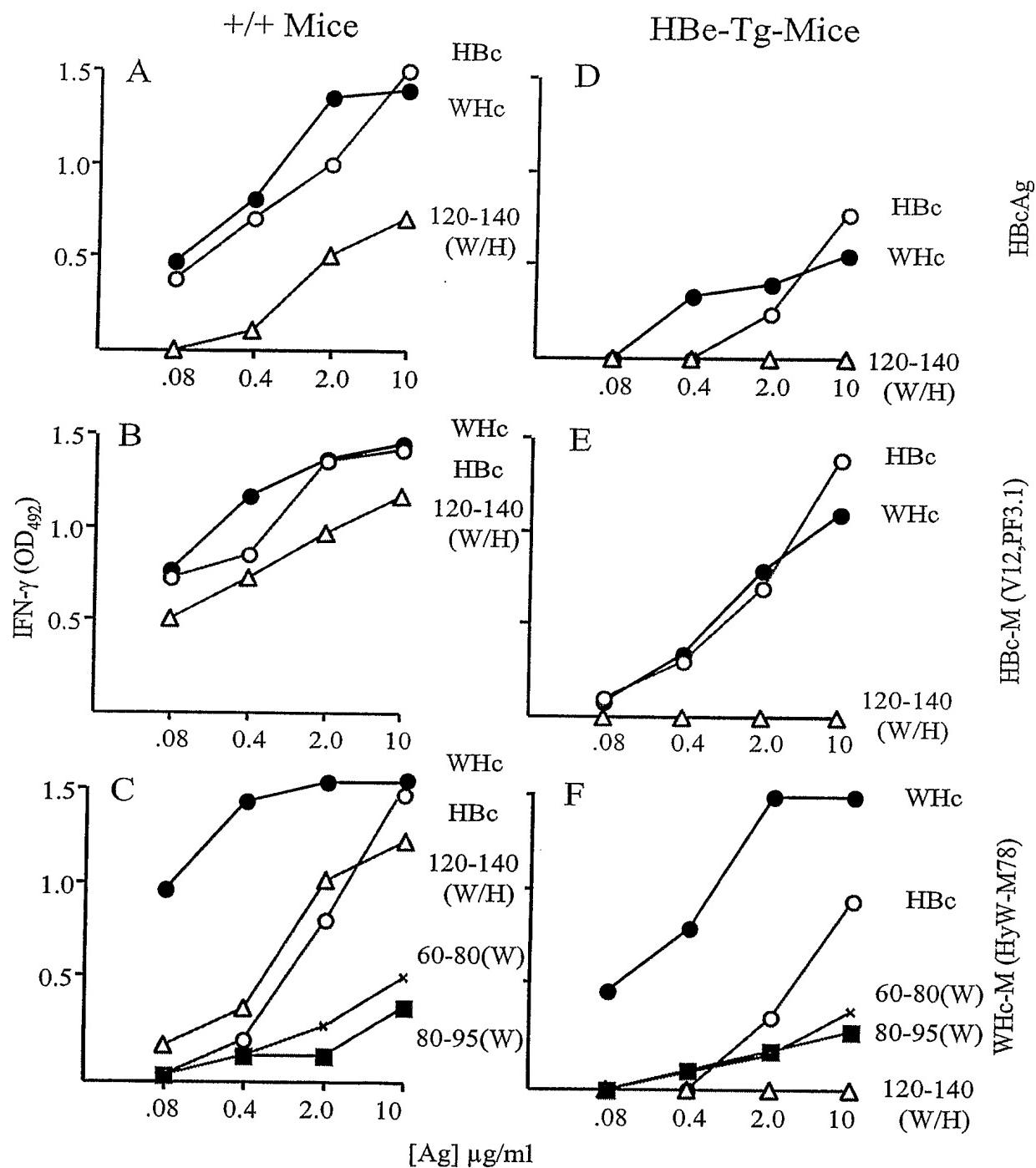


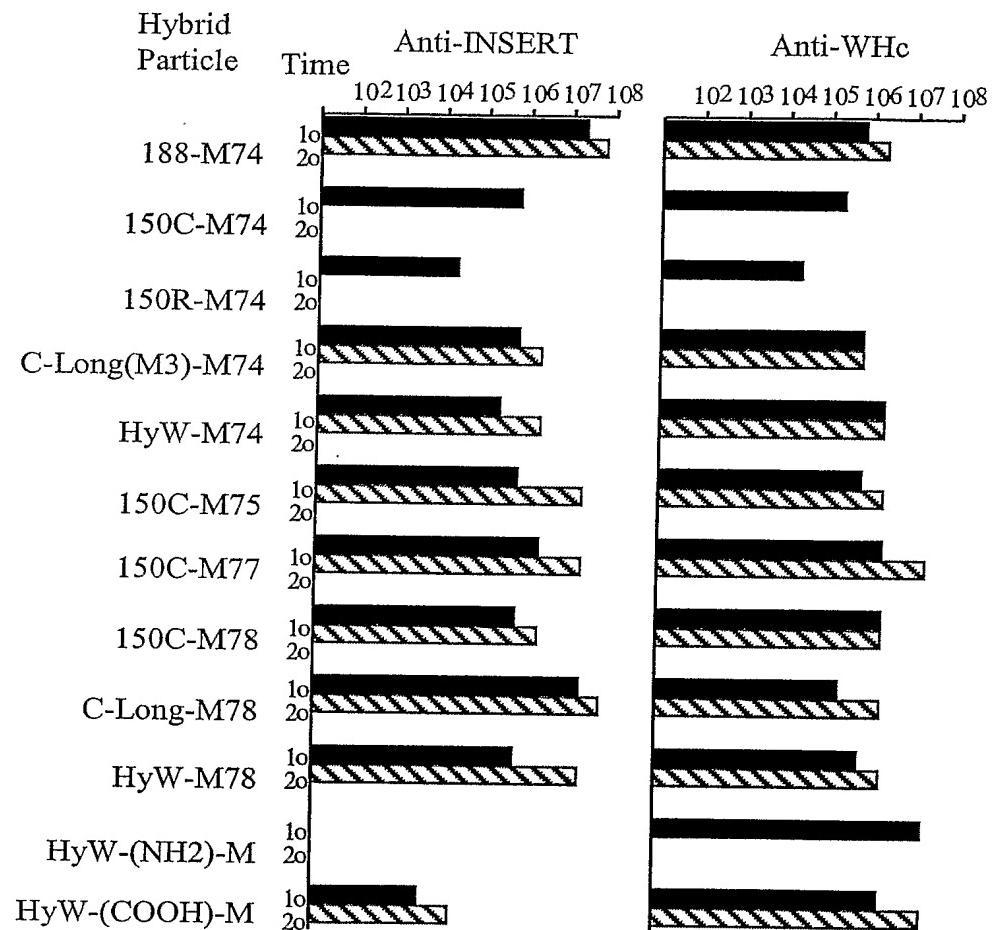
Fig. 9

**Fig. 10**

**Fig. 11**

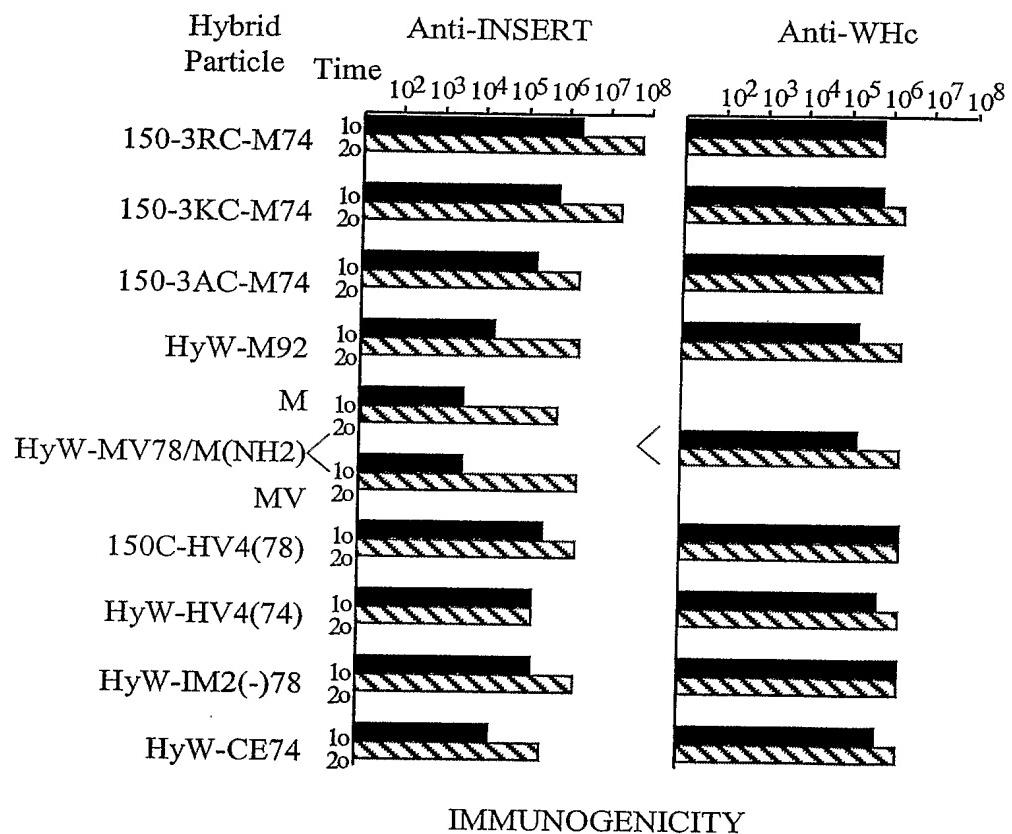
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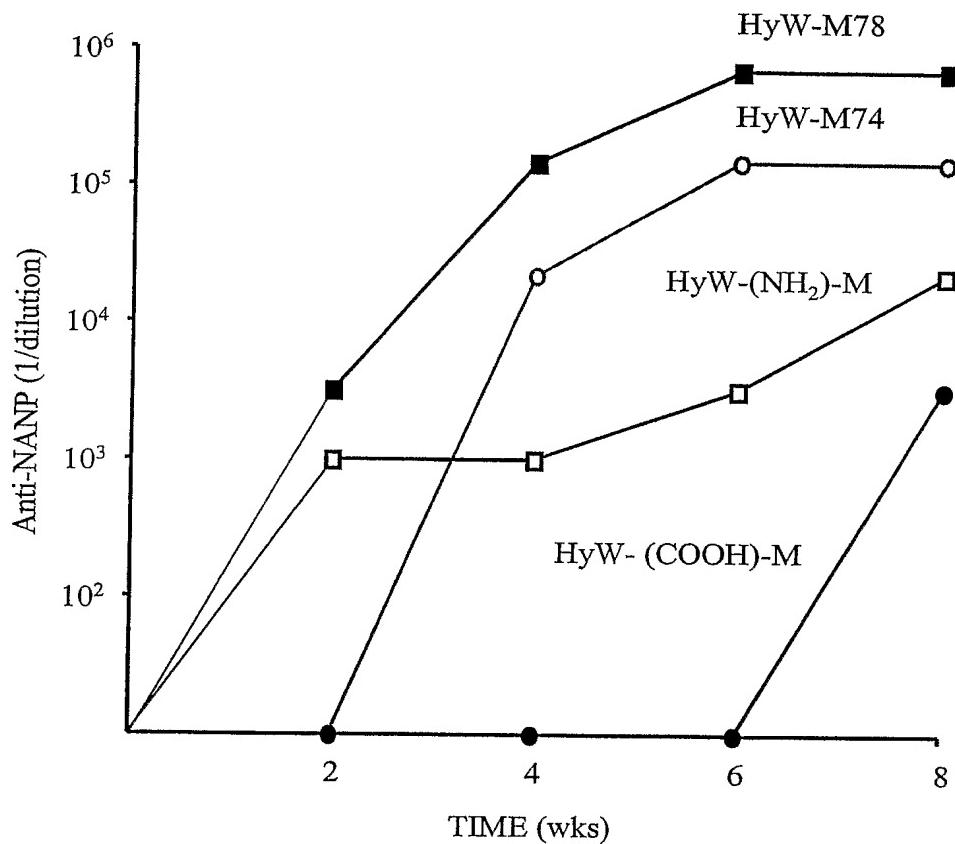
**Fig. 13**



IMMUNOGENICITY

Fig. 14

**Fig. 15**

**Fig. 16**

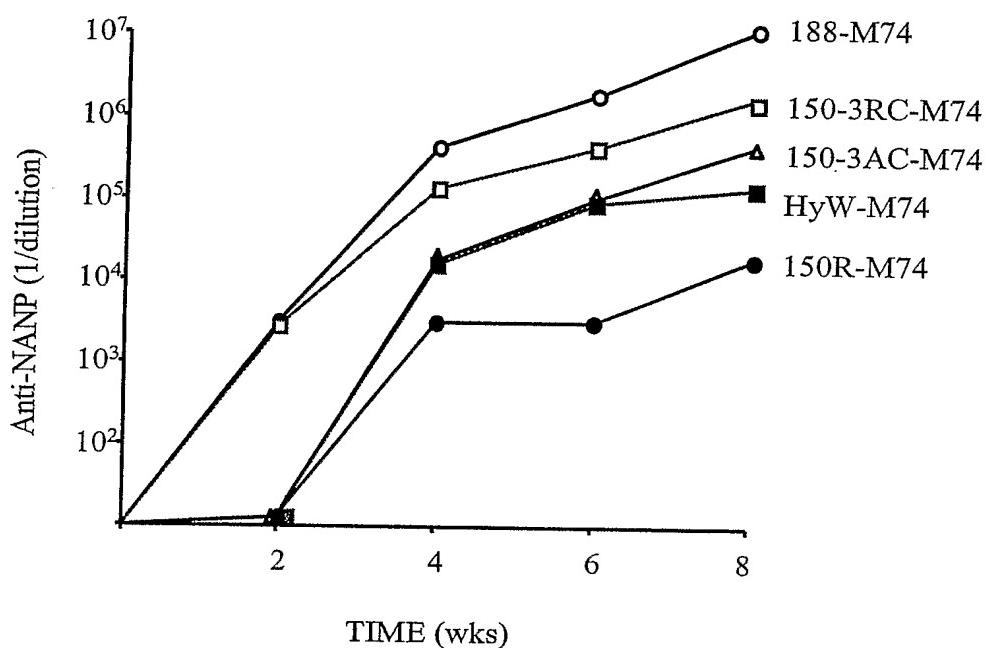
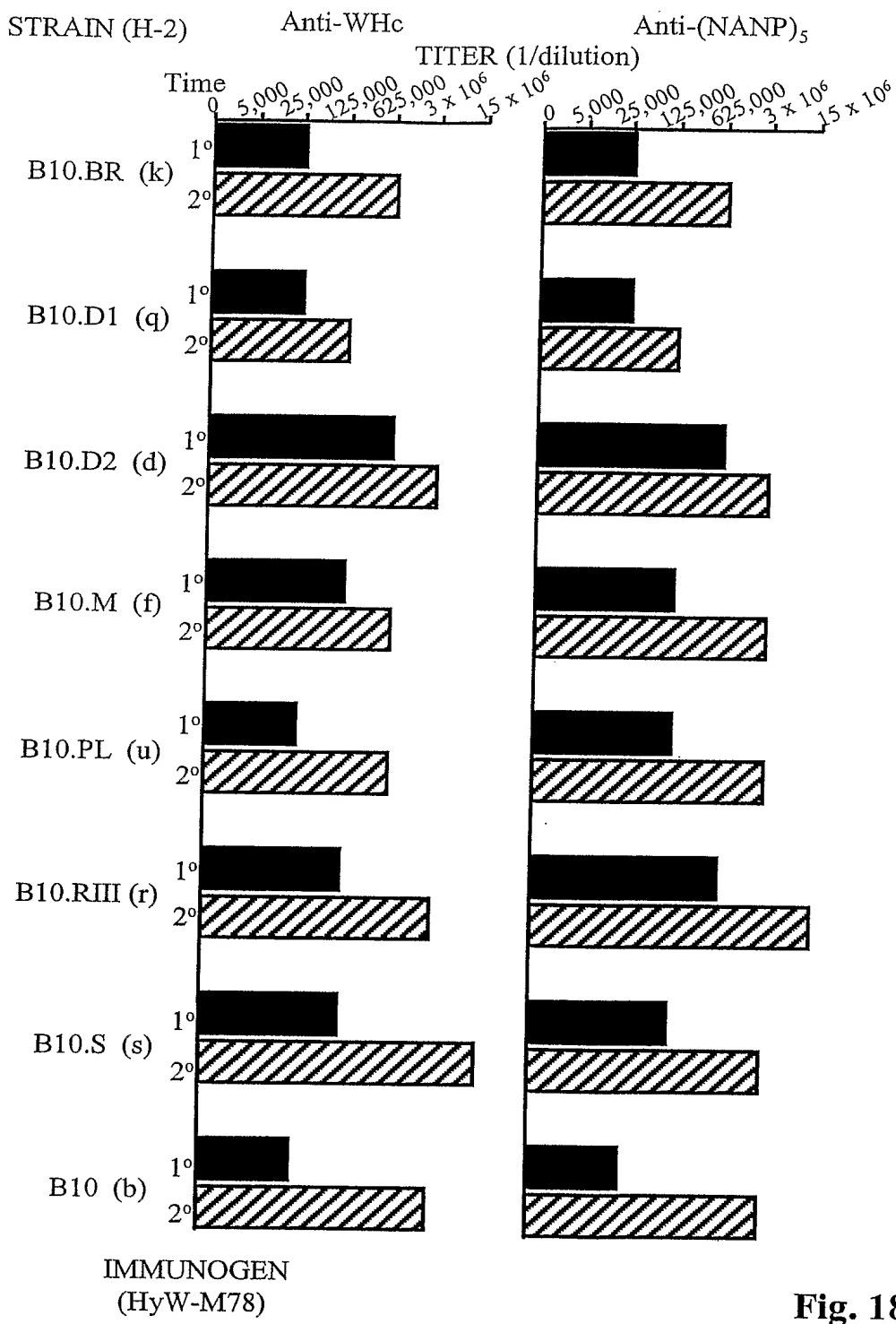
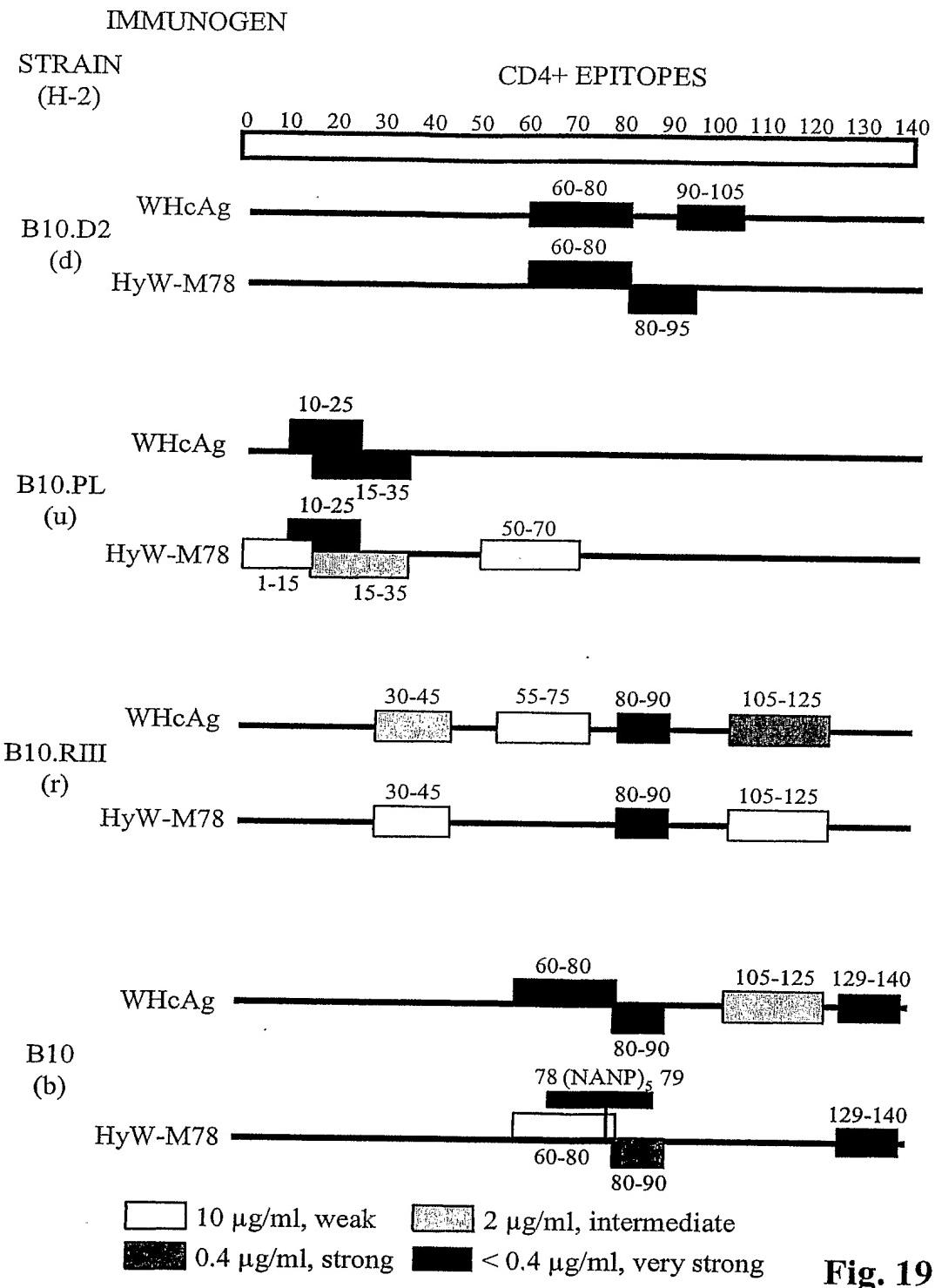
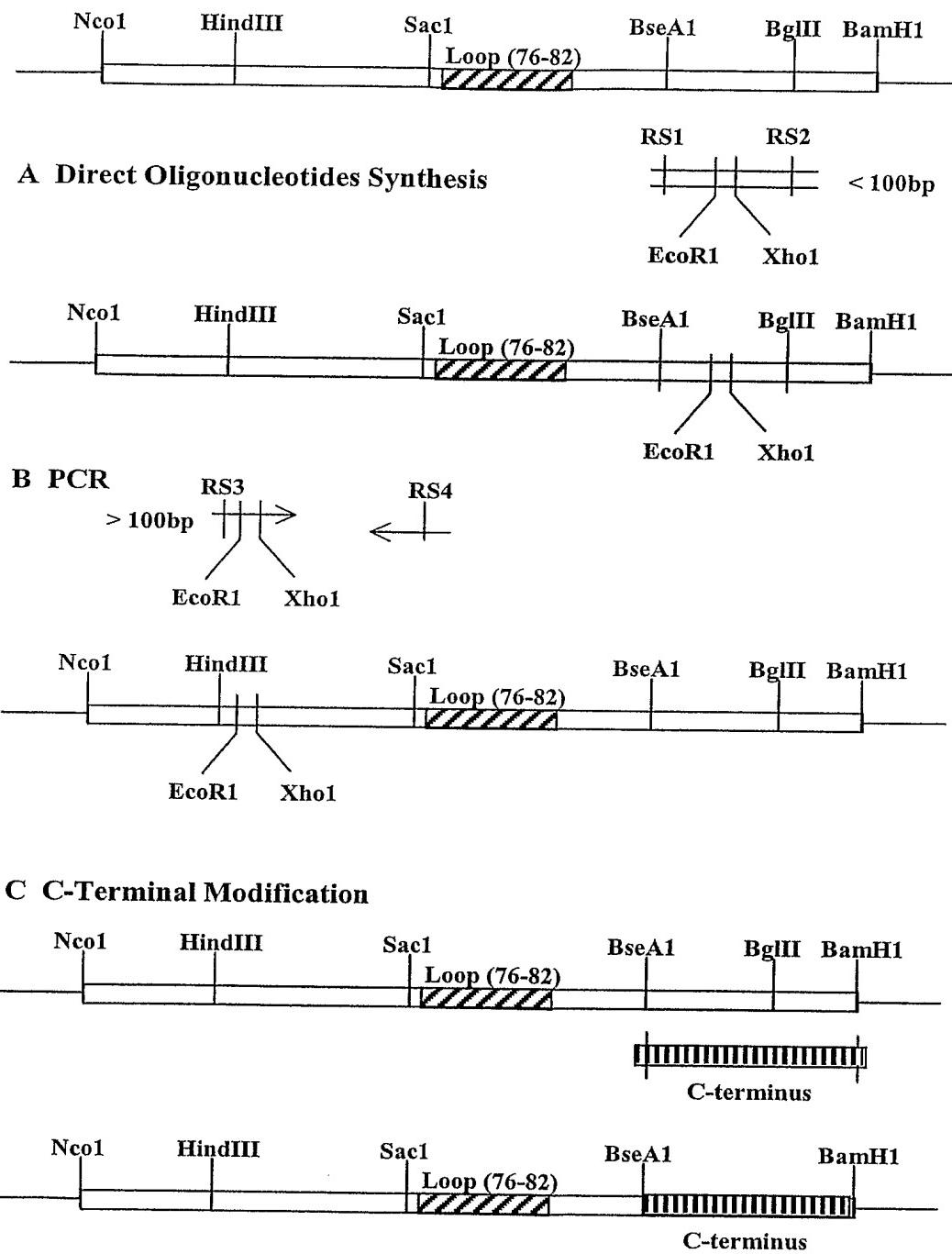
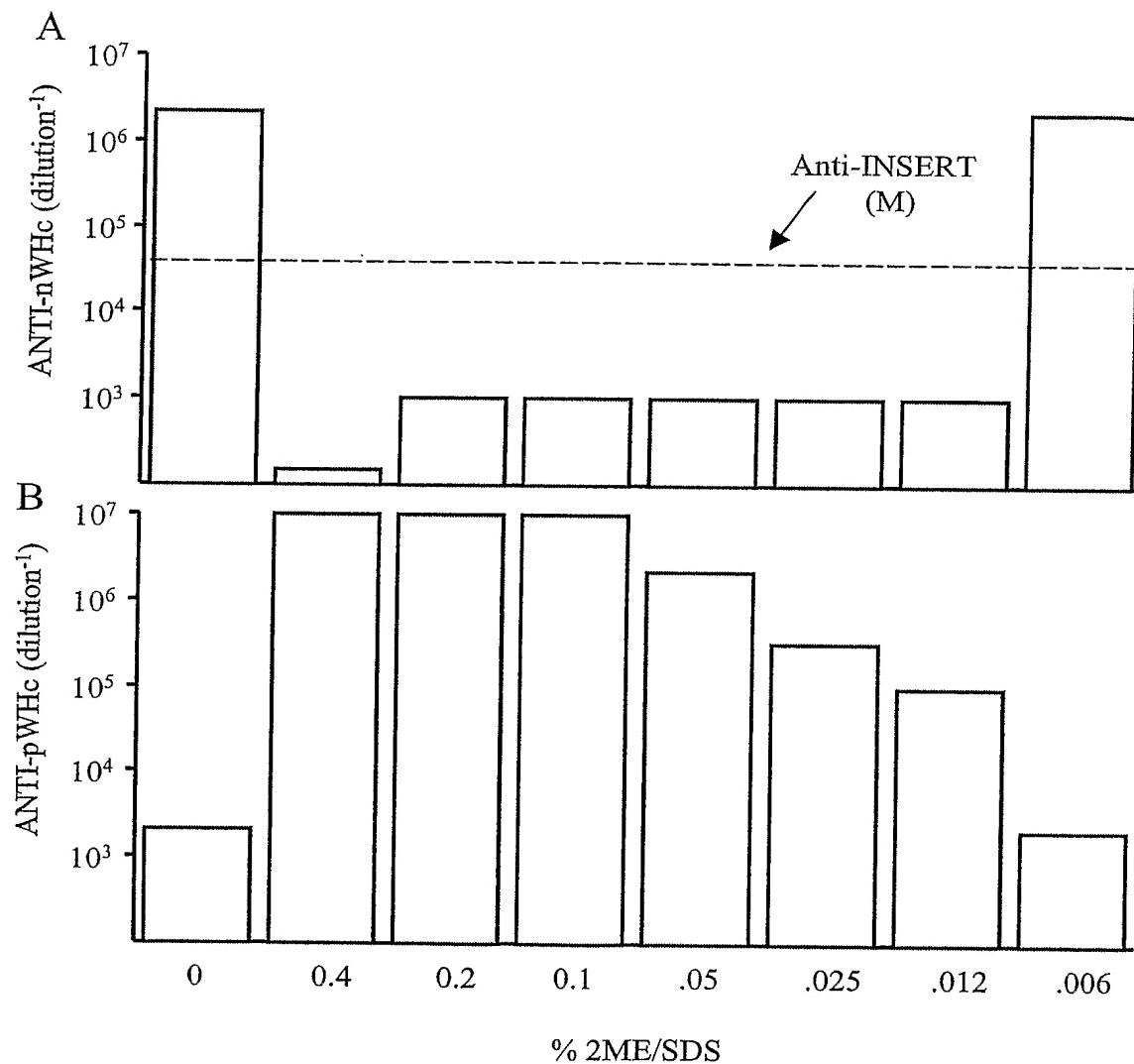


Fig. 17

**Fig. 18**

**Fig. 19**

**Fig. 20**

**Fig. 21**

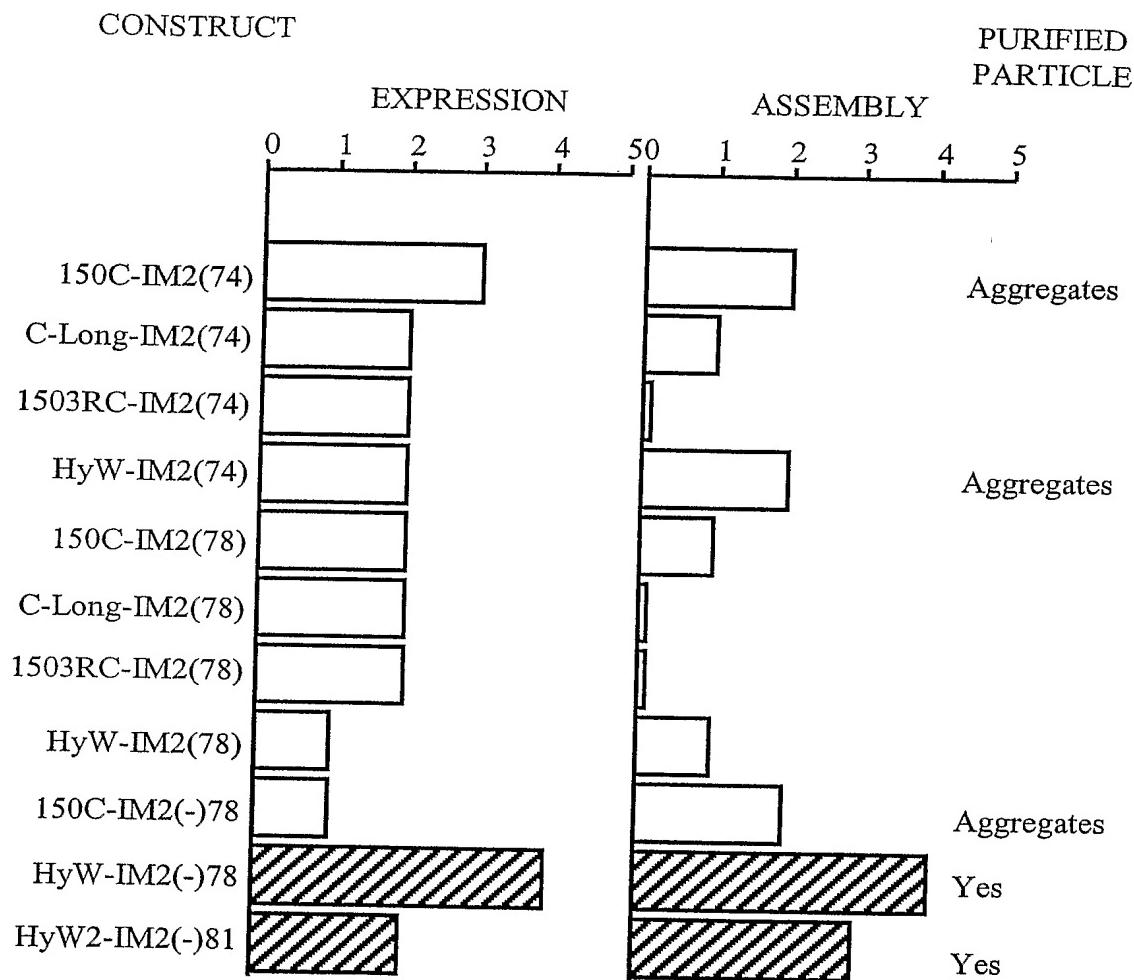
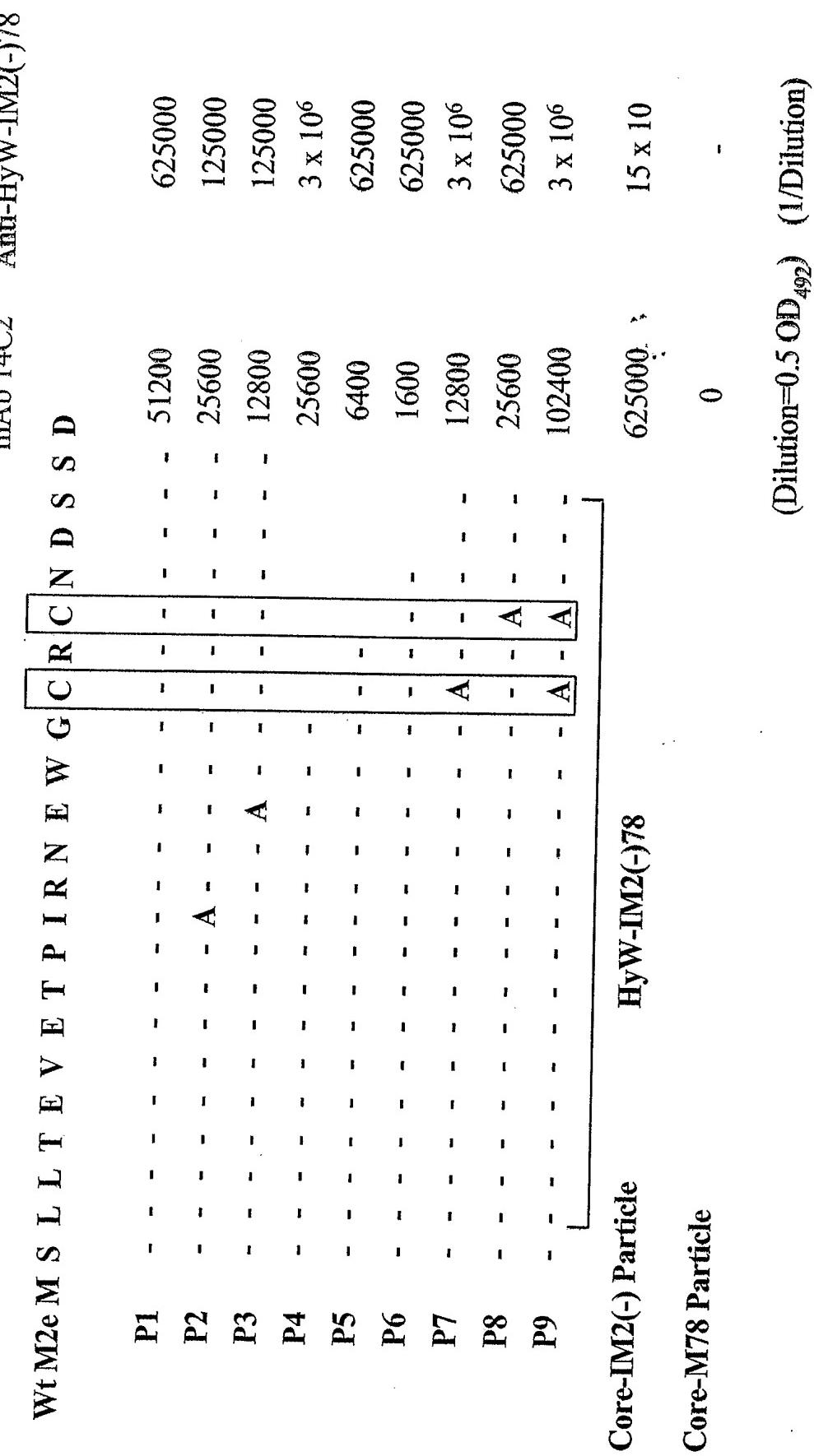
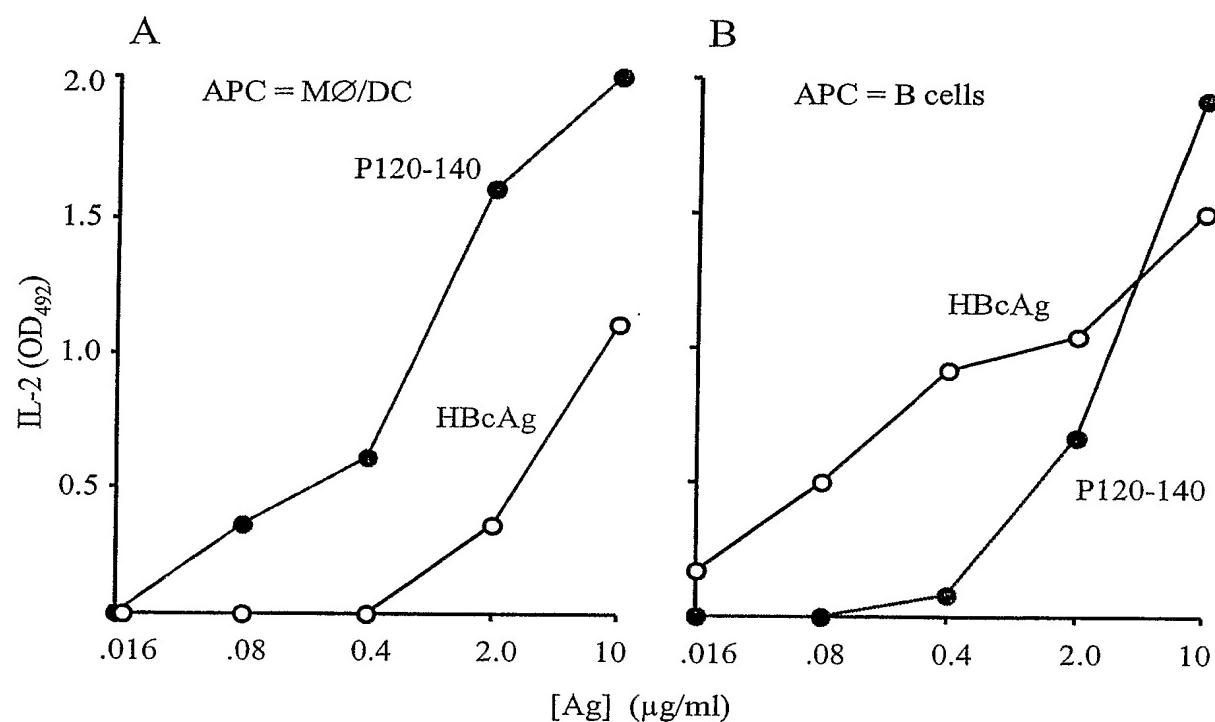
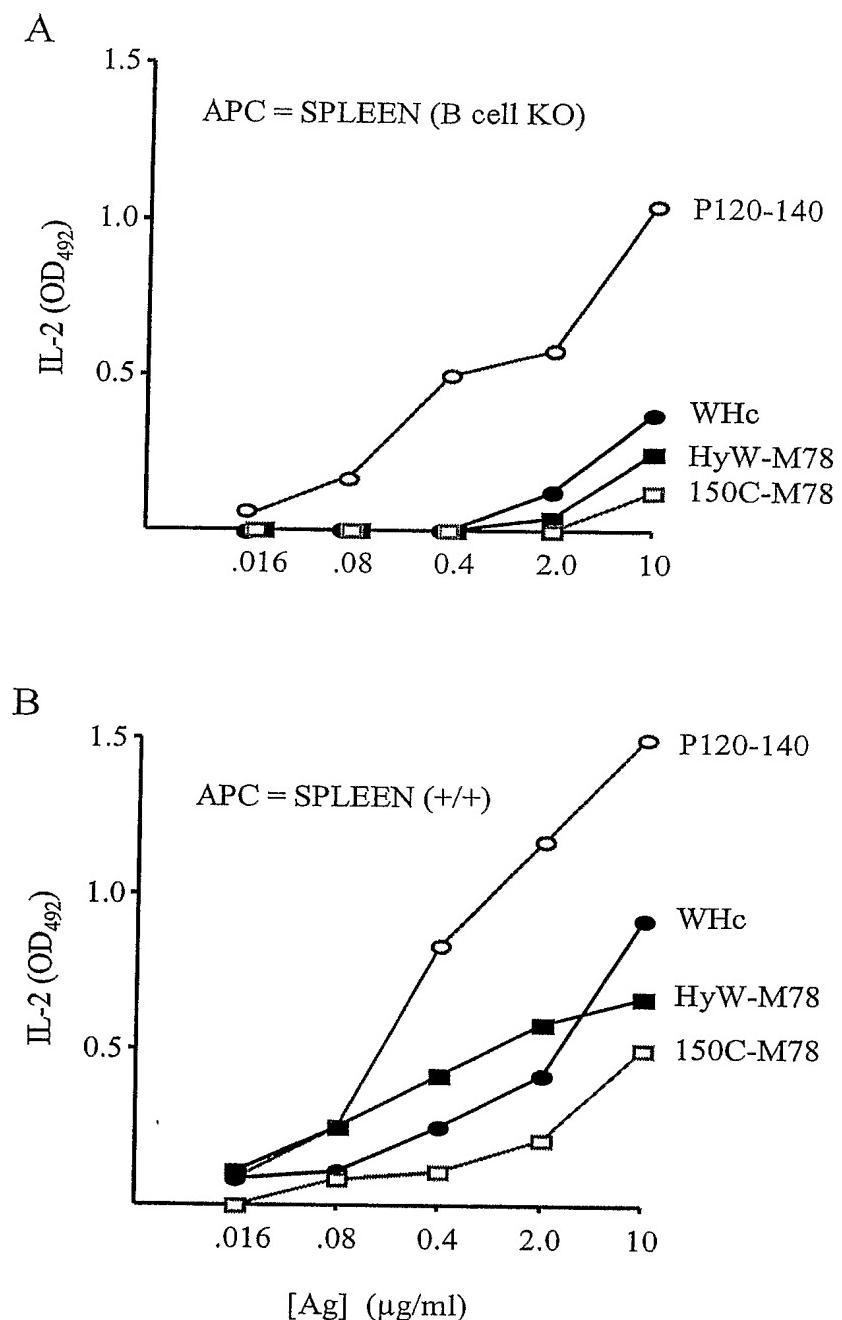
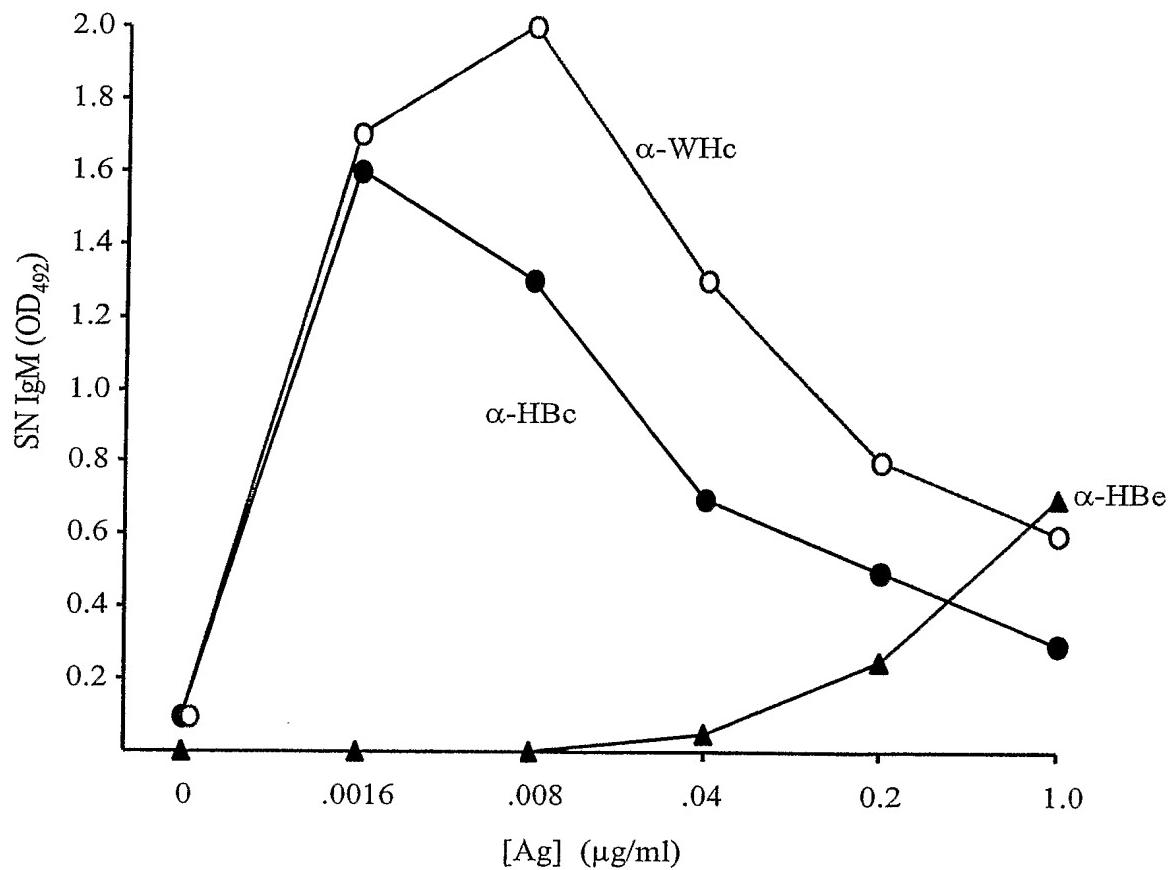
**Fig. 22**

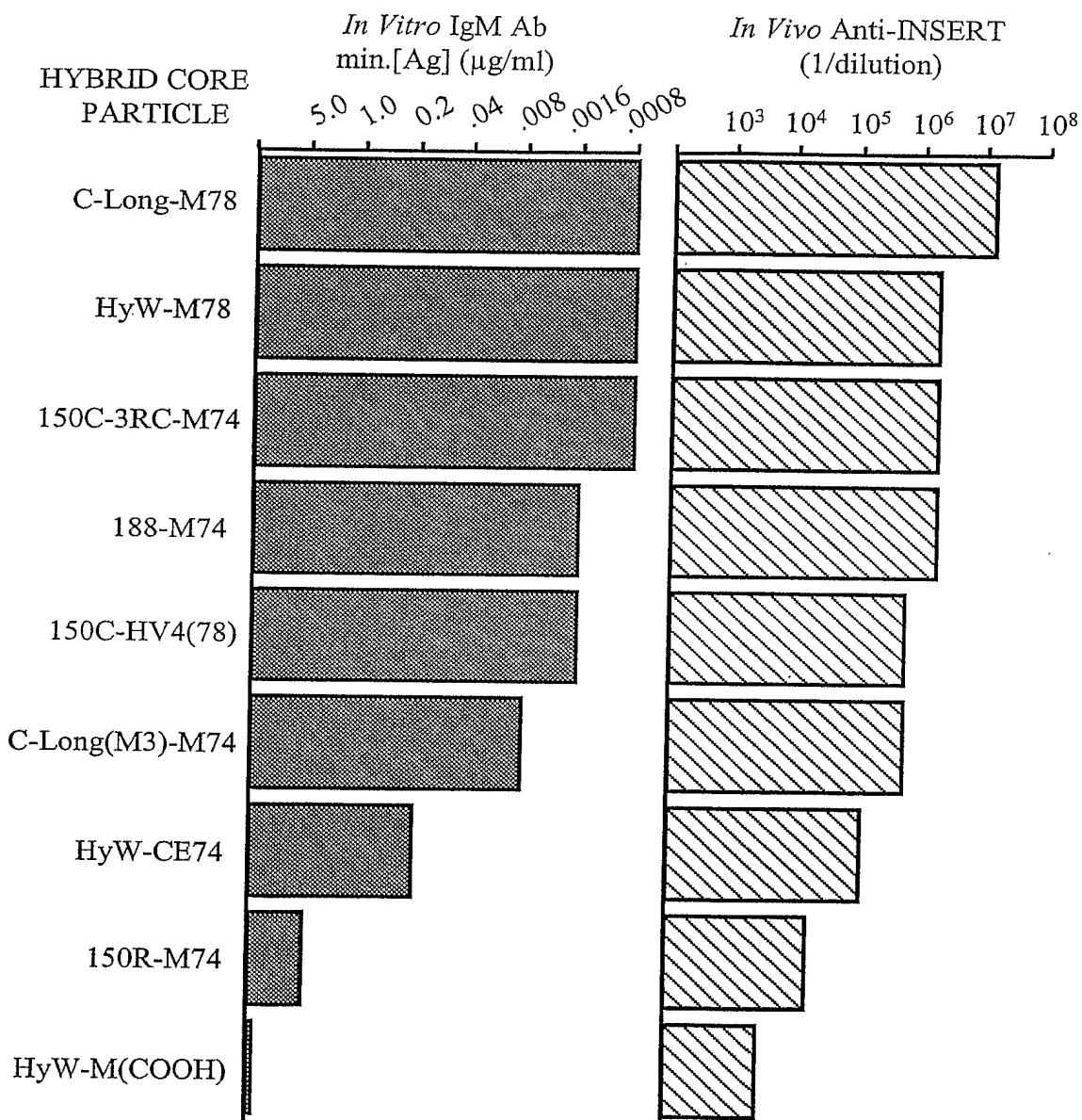
Fig. 23

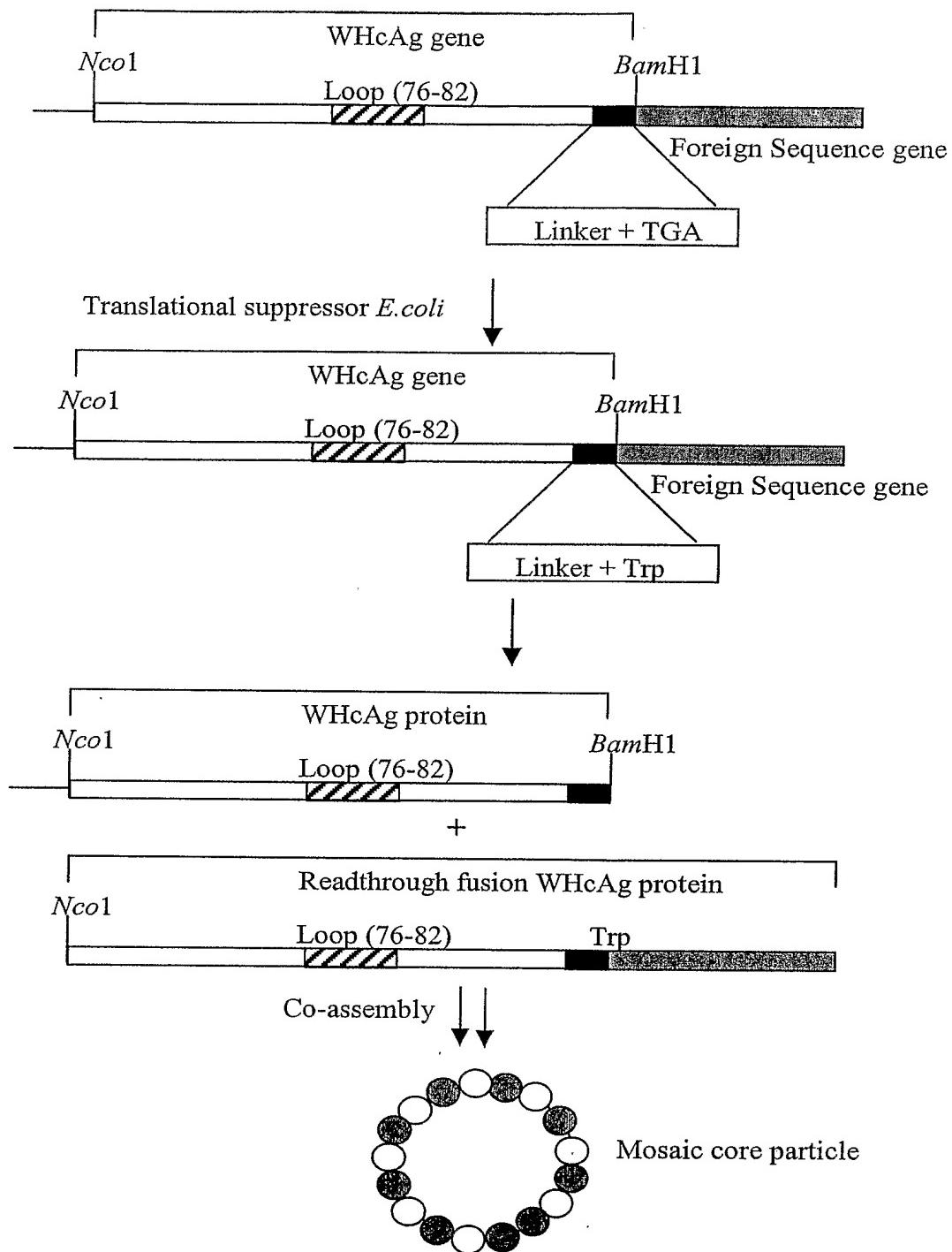


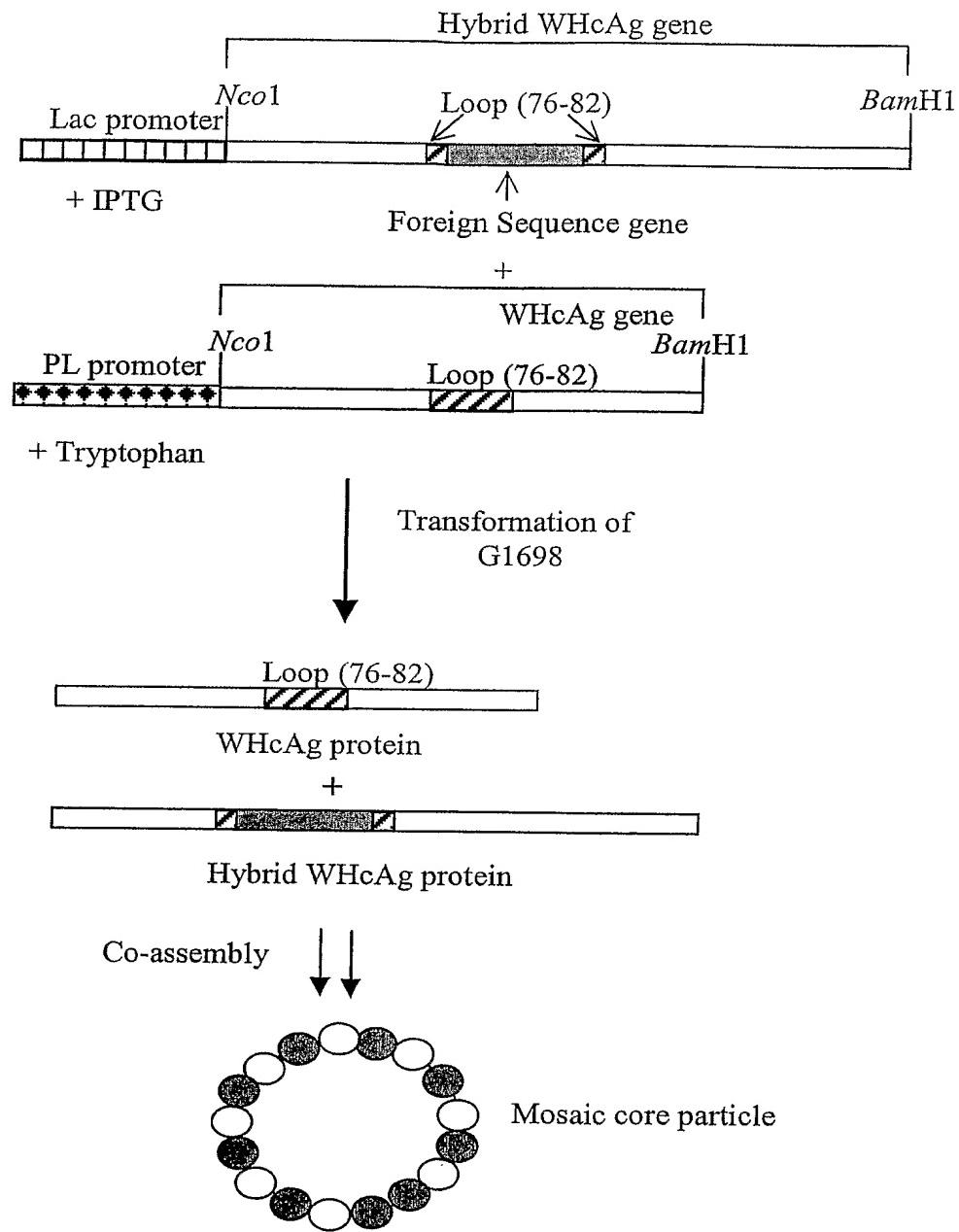
**Fig. 24**

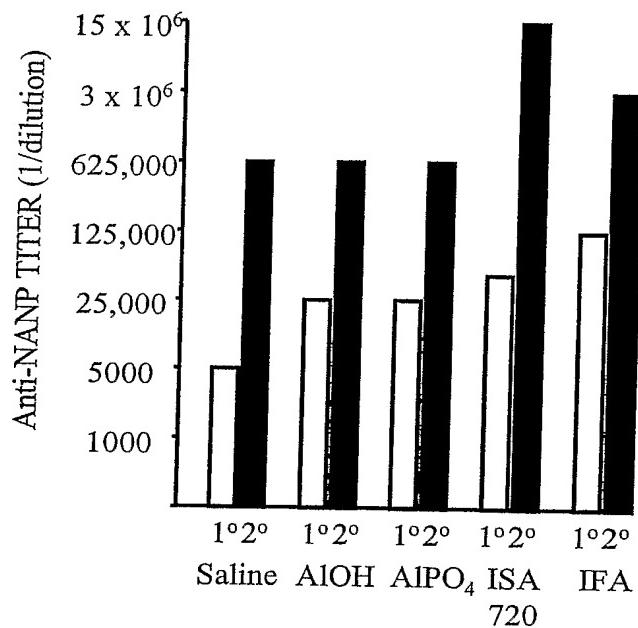
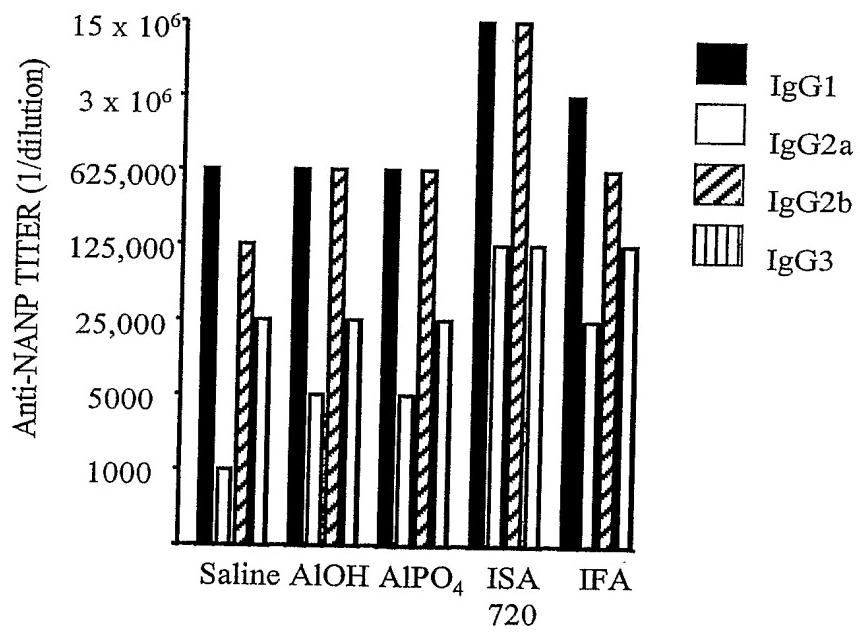
**Fig. 25**

**Fig. 26**

**Fig. 27**

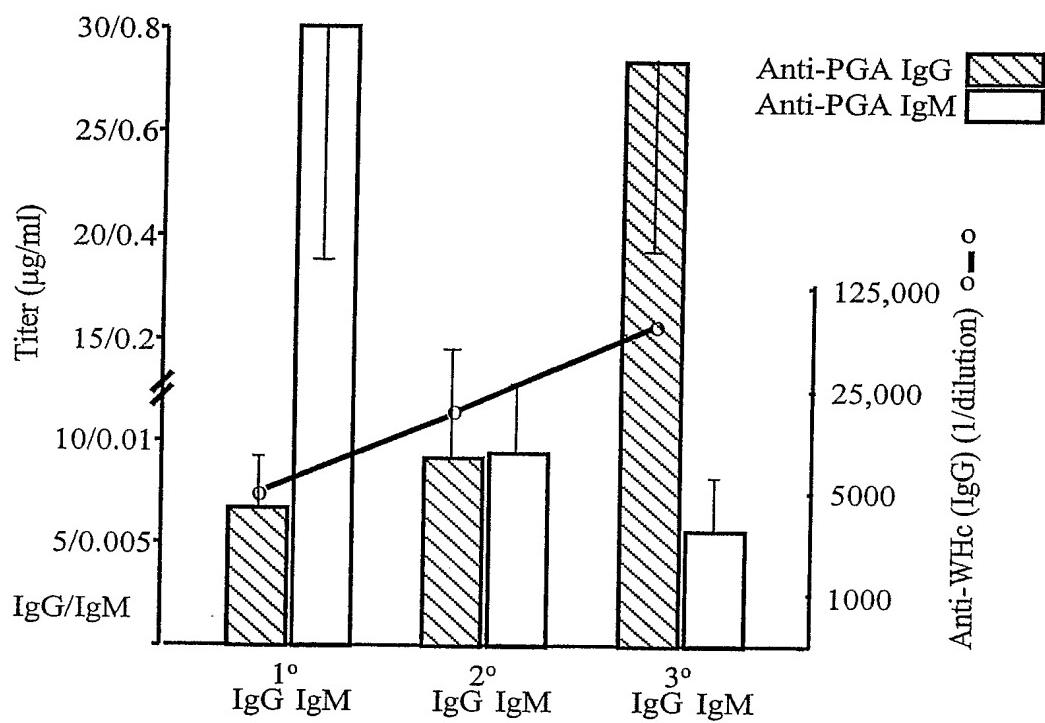
**Fig. 28**

**Fig. 29**

A**B**

Adjuvant

Fig. 30

**Fig. 31**

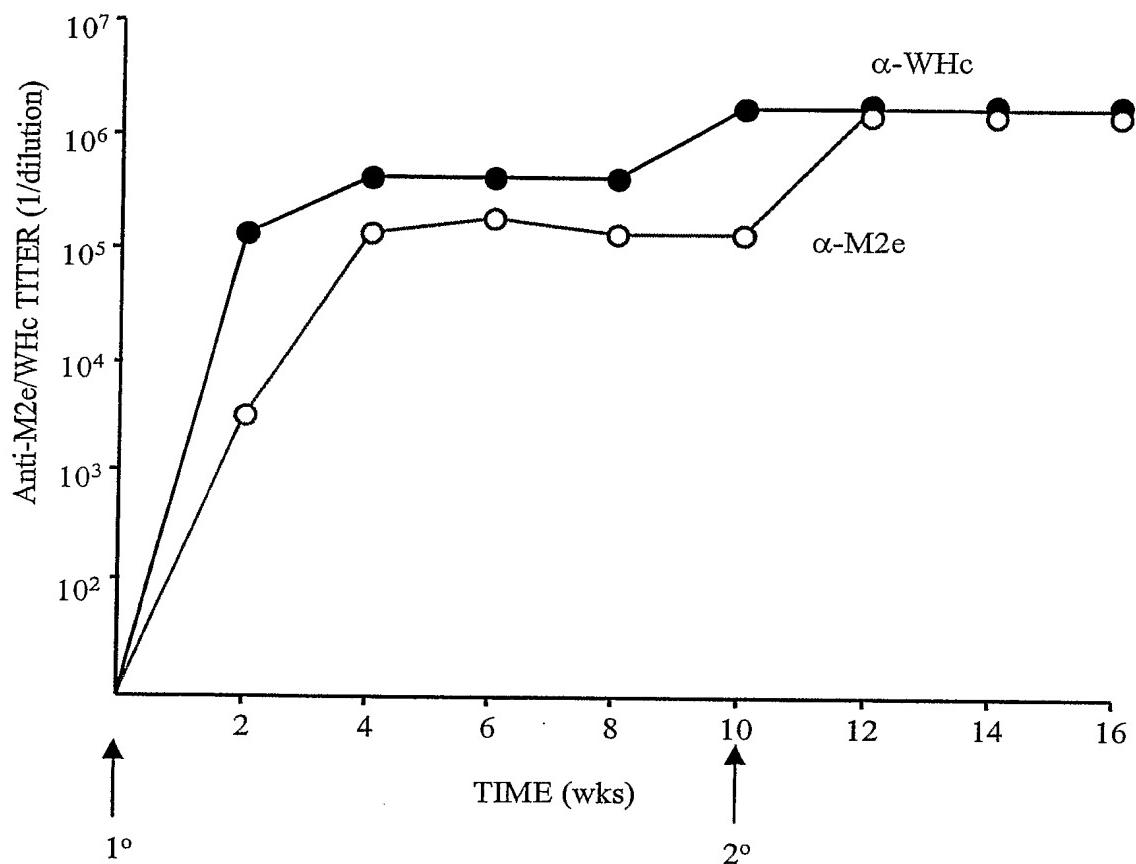


Fig. 32

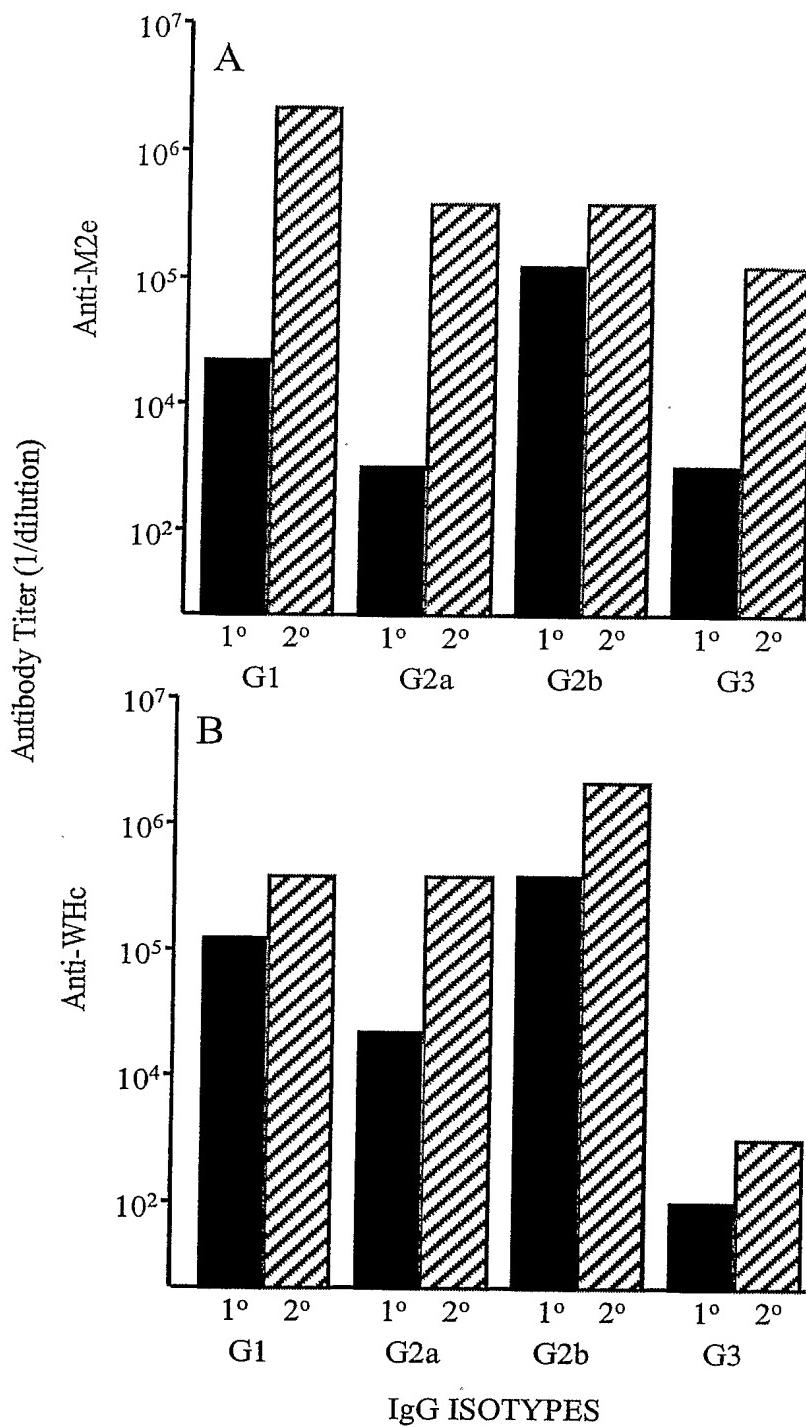


Fig. 33

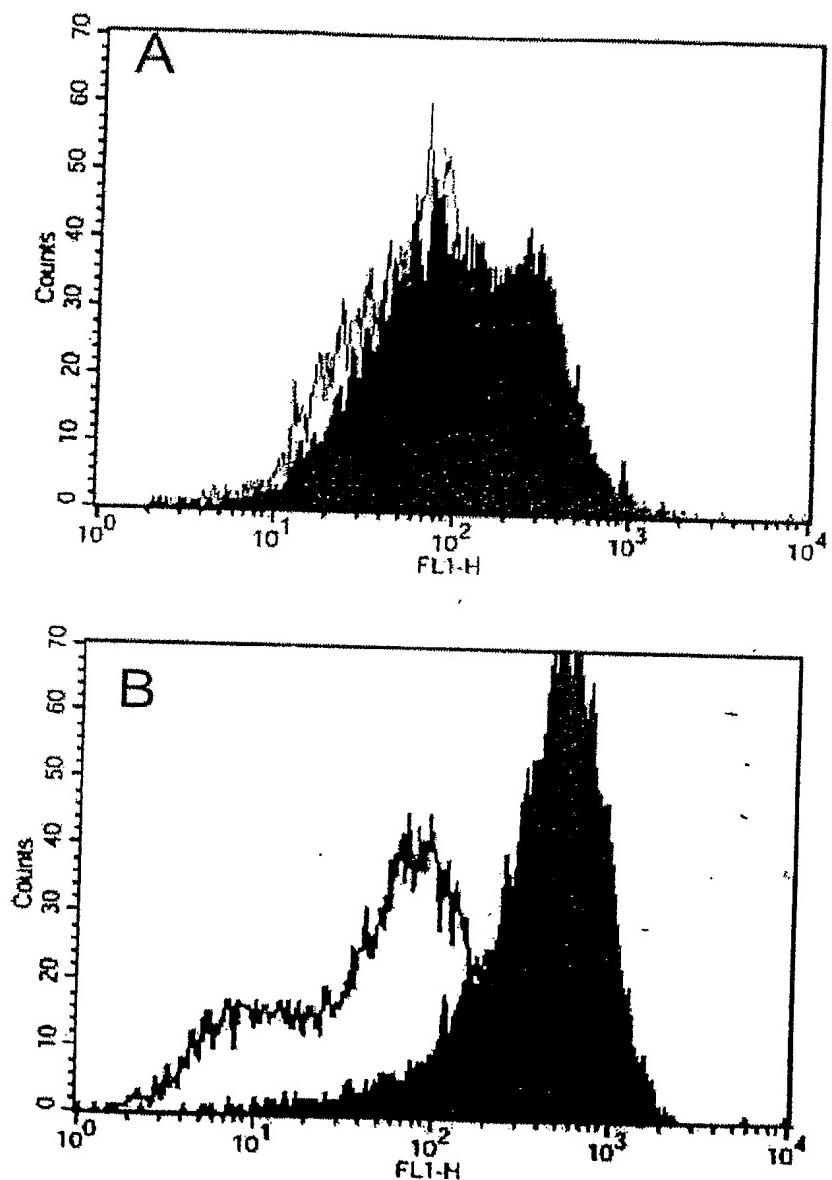
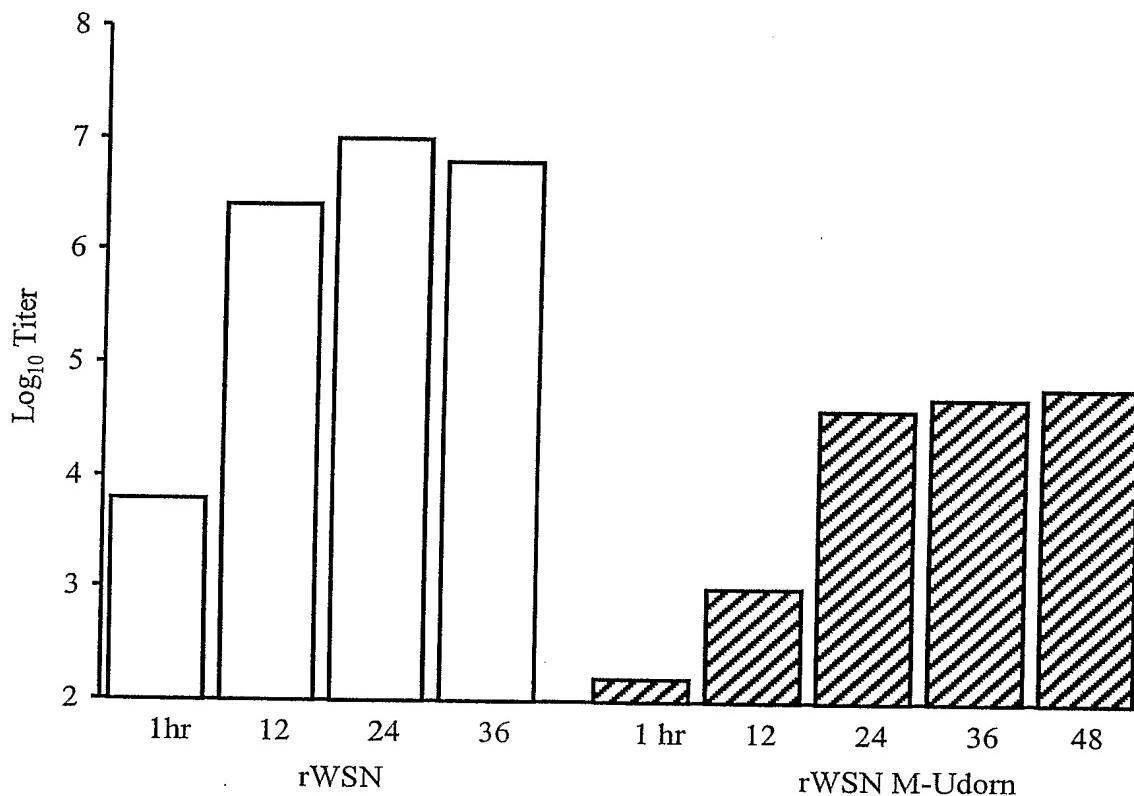


Fig. 34

**Fig. 35**

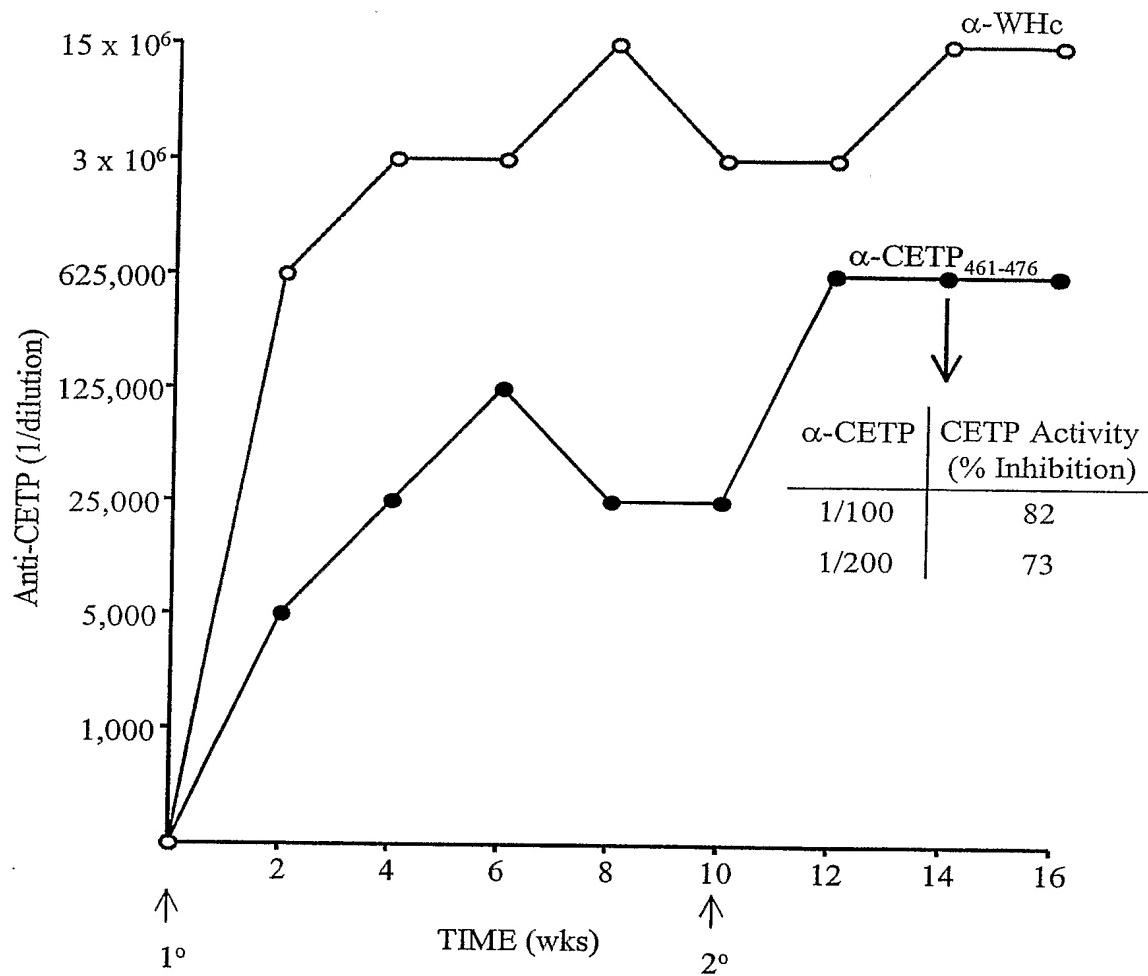
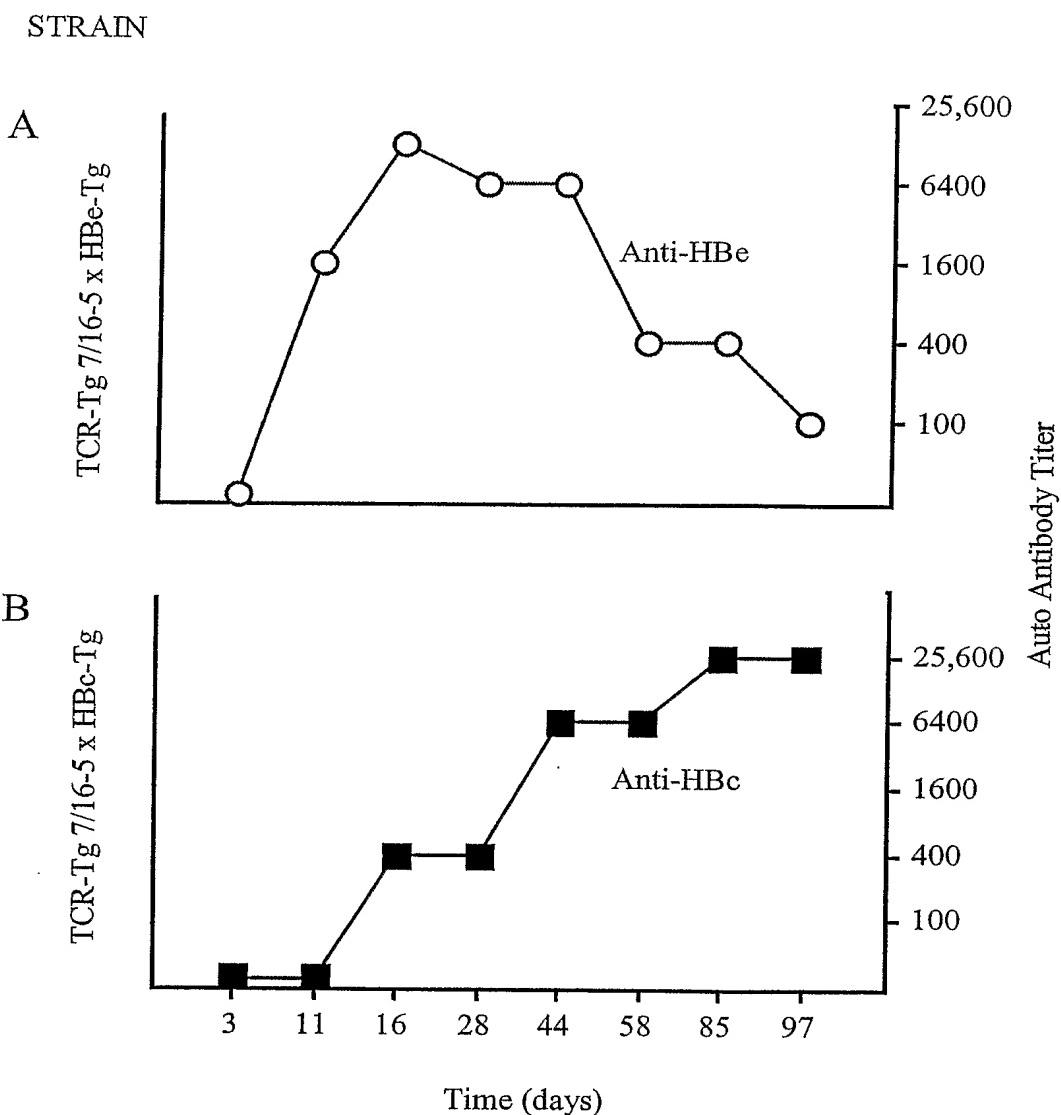


Fig. 36

**Fig. 37**

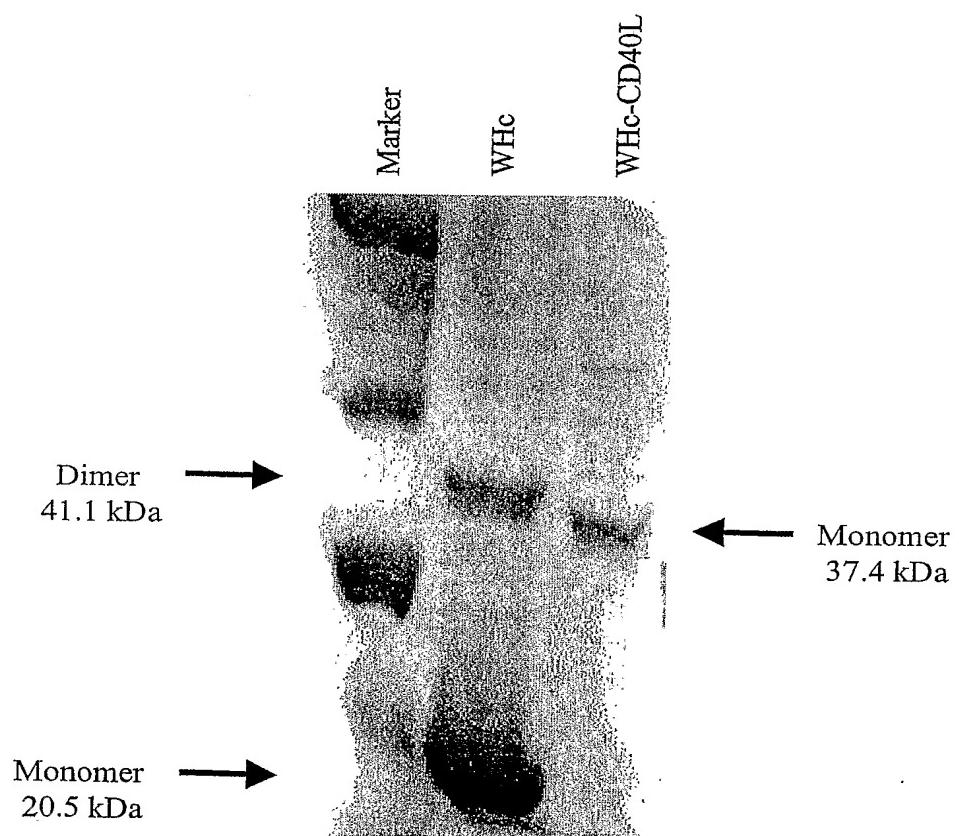


Fig. 38

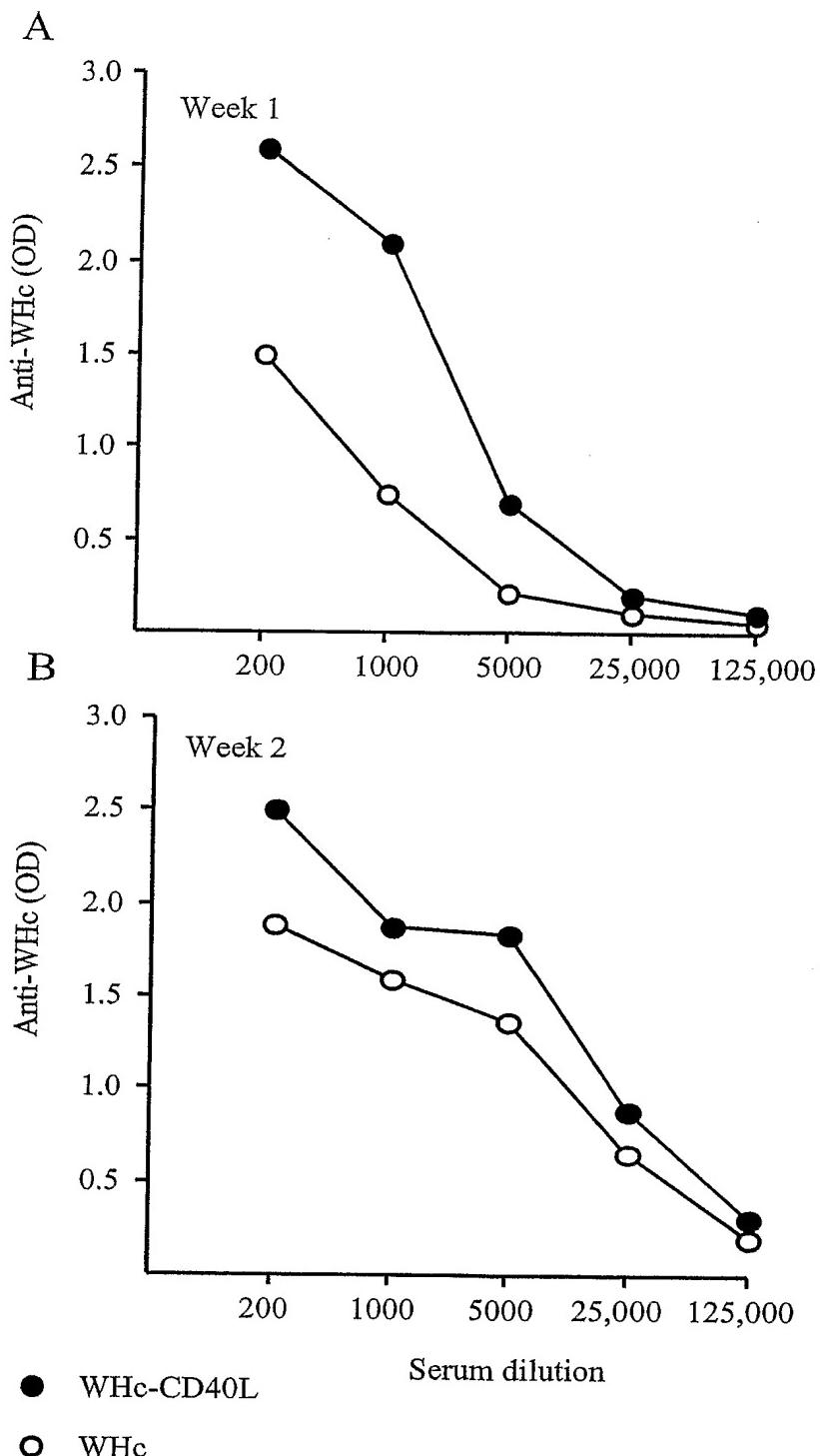
**Fig. 39**

Fig. 40**A Wild Type WHcAg DNA (SEQ ID NO:37)**

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TTTGGACTTCTTCCTGACCTTAATGCTTGTTGGACACTGCTACTGCCTGTATGAAG  
AAGAGCTAACAGGTAGGAAACATTGCTCTCCGCACCATAACAGCTATTAGACAAGCTTA  
GTATGCTGGGATGAATTAACTAAATTGATAGCTTGGATGAGCTCTAACATAACTTCTGA  
ACAAGTAAGAACAACTATTGTAATCATGTCAATGATACTGGGACTTAAGGTGAGAC  
AAAGTTTATGGTTTCATTGTCAATGTCTCACTTCGGACAAACATAACAGTTCAAGAATT  
TTAGTAAGTTTGGAGTATGGATCAGGACTCCAGCTCCATATAGACCTCCTAATGCACC  
CATTCTCTCGACTCTCCGGAACATAACAGTCATTAGGAGAAGAGGAGGTGCAAGAGCTT  
CTAGGTCCCCCAGAACAGACGCACTCCCTCCTCGCAGGAGAAGATCTCAATCACCGCGT  
CGCAGACGCTCTCAATCTCCATCTGCCAACTGCTGA
```

B Wild Type WHcAg (SEQ ID NO:1)

```
MDIDPYKEFGSSYQLLNFLPLDFFPDLNALVDTATALYEEELTGREHCSPHHTAIRQAL  
VCWDELTKLIAWMSSNITSEQVRTIIVNHVNDTWGLKVRQSLWFHLSCLTFQHTVQEF  
LVSFGVWIRTPAPYRPPNAPISTLPEHTVIRRRGGARASRSPRRRTSPRRRSQSPR  
RRRSQSPSANC
```

C Truncated WHcAg (SEQ ID NO:38)

```
MDIDPYKEFGSSYQLLNFLPLDFFPDLNALVDTATALYEEELTGREHCSPHHTAIRQAL  
VCWDELTKLIAWMSSNITSEQVRTIIVNHVNDTWGLKVRQSLWFHLSCLTFQHTVQEF  
LVSFGVWIRTPAPYRPPNAPISTLPEHTVI
```

Fig. 41**A Wild Type GSHcAg DNA (SEQ ID NO:39)**

```
ATGGACATAGATCCCTATAAAGAATTGGTTCTTATCAGTTGTTGAATTTCTTCC
TTGGACTTTTCCTGATCTCAATGCATTGGTGGACACTGCTGCTGCTTTATGAAG
AAGAATTAACAGGTAGGGAGCATTGTTCTCCTCATCATACTGCTATTAGACAGGCCTTA
GTGTGTTGGGAAGAATTAACTAGATTAATTACATGGATGAGTGAAAATACAACAGAAAGA
AGTTAGAAGAATTATTGTTGATCATGTCAATAATACTTGGGGACTTAAAGTAAGACAGA
CTTATGGTTTCATTTATCATGTCTTACTTTGGACAACACACAGTTCAAGAATTTTG
GTTAGTTTGGAGTATGGATTAGAACTCAGCTCCTTATAGACCACCTAATGCACCCAT
TTTATCAACTCTCCGGAACATACAGTCATTAGGAGAAGAGGGAGGTTCAAGAGCTGCTA
GGTCCCCCGAAGACGCACTCCCTCTCGCAGGAGAAGGTCTCAATCACCGCGTCGC
AGACGCTCTCAATCTCCAGCTTCCAAGTGTGA
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B Wild Type GSHcAg (SEQ ID NO:21)

```
MDIDPYKEFGSSYQLLNFLPLDFFPDLNALVDTAAALYEEELTGREHCSPHHTAIRQAL
VCWEELTRLITWMSENTTEEVRIIVDHVNNTWGLKVRQTLWFHLSCLTFGQHTVQEFL
VSFGVWIRTPAPYRPPNAPILSTLPEHTVIRRGGSRAARSPRRRTSPRRRSQSPRR
RRSQSPASNC
```

C Truncated GSHcAg (SEQ ID NO:40)

```
MDIDPYKEFGSSYQLLNFLPLDFFPDLNALVDTAAALYEEELTGREHCSPHHTAIRQAL
VCWEELTRLITWMSENTTEEVRIIVDHVNNTWGLKVRQTLWFHLSCLTFGQHTVQEFL
VSFGVWIRTPAPYRPPNAPILSTLPEHTVI
```

Fig. 42

A Wild Type HBcAg DNA (SEQ ID NO:57)

```
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AAGCCTTAGAGTCTCCTGAGCATTGTCACCTCACCAACTGCACTCAGGCAAGCAATT
CTTGCTGGGGGAACTAATGACTCTAGCTACCTGGGTGGGTGTTAATTGGAAGATCC
AGCATCCAGAGACCTAGTAGTCAGTTATGTCAACACTAATATGGGCCTAAAGTCAGGC
AACTCTTGTGGTTCACATTCTGTCTCACTTTGGAAGAGAAACCGTTATAGAGTAT
TTGGTGTCTTCGGAGTGTGGATTCGCACTCCTCAGCTTATAGACGACGAGGCAGGTCCCCTAGAA
TATCCTATCAACACTCCGGAAACTACTGTTAGACGACGAGGCAGGTCCCCTAGAA
GAAGAACTCCCTCGCCTCGCAGACGAAGGTCTCAATGCCCGTGCAGAAGATCTCAA
TCTCGGAATCTCAATGTTGA
```

B Wild Type HBcAg (SEQ ID NO:41)

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MDIDPYKEFGATVELLSFLPSDFFPSVRDLLDTASALYREALESPEHCSPHHTALRQAI
LCWGEELMTLATWGVNLEDPASRDLVVSYVNTNMGLKFRQLLWFHISCLTFGRETVIEY
LVSFGVWIRTPPAYRPPNAPILSTLPETTVVRRGRSPRRRTSPRRRSQSPRRRSQSRESQC
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C Truncated HBcAg (SEQ ID NO:58)

```
MDIDPYKEFGATVELLSFLPSDFFPSVRDLLDTASALYREALESPEHCSPHHTALRQAI54
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LVSFGVWIRTPPAYRPPNAPILSTLPETTVV
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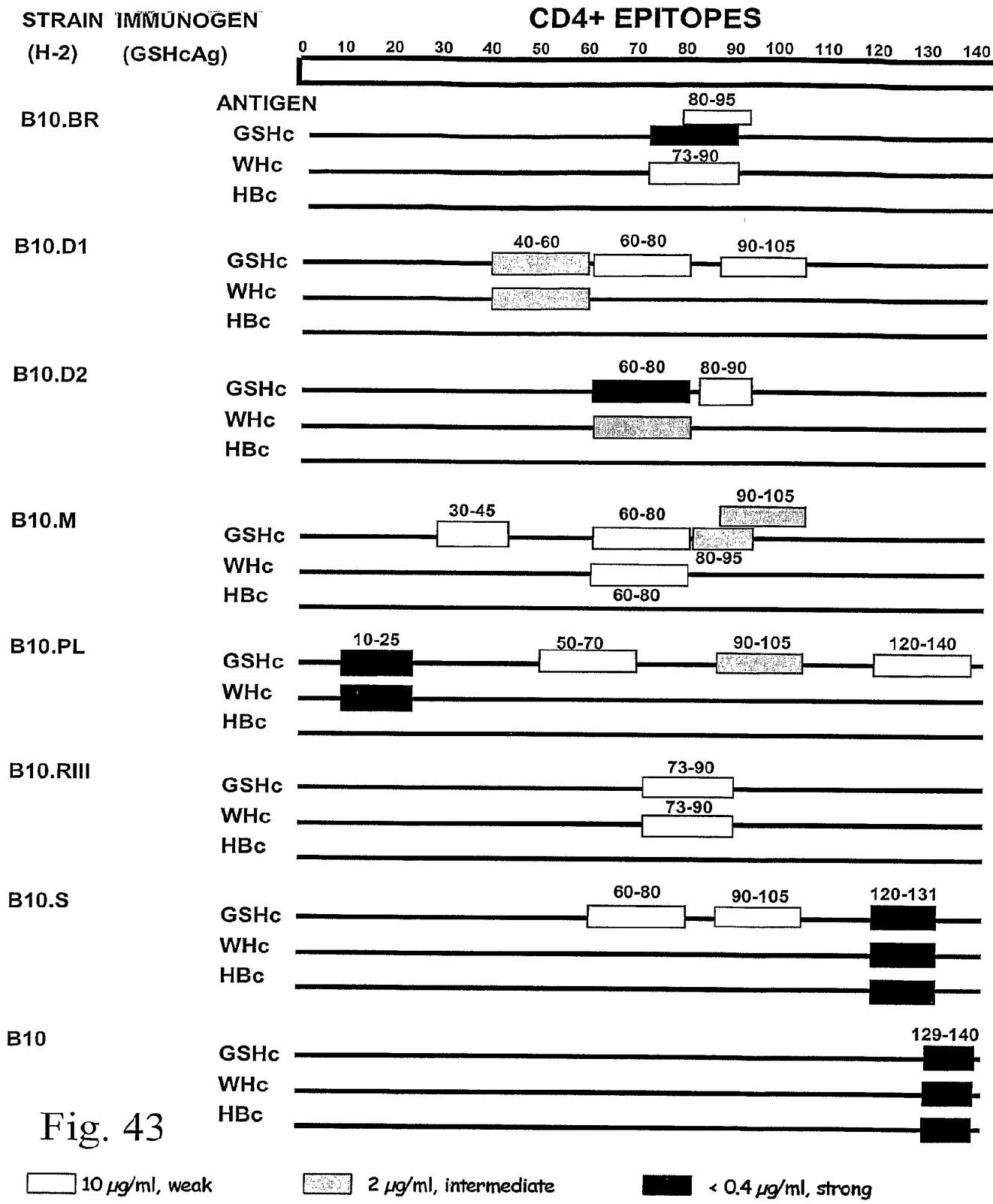


Fig. 43

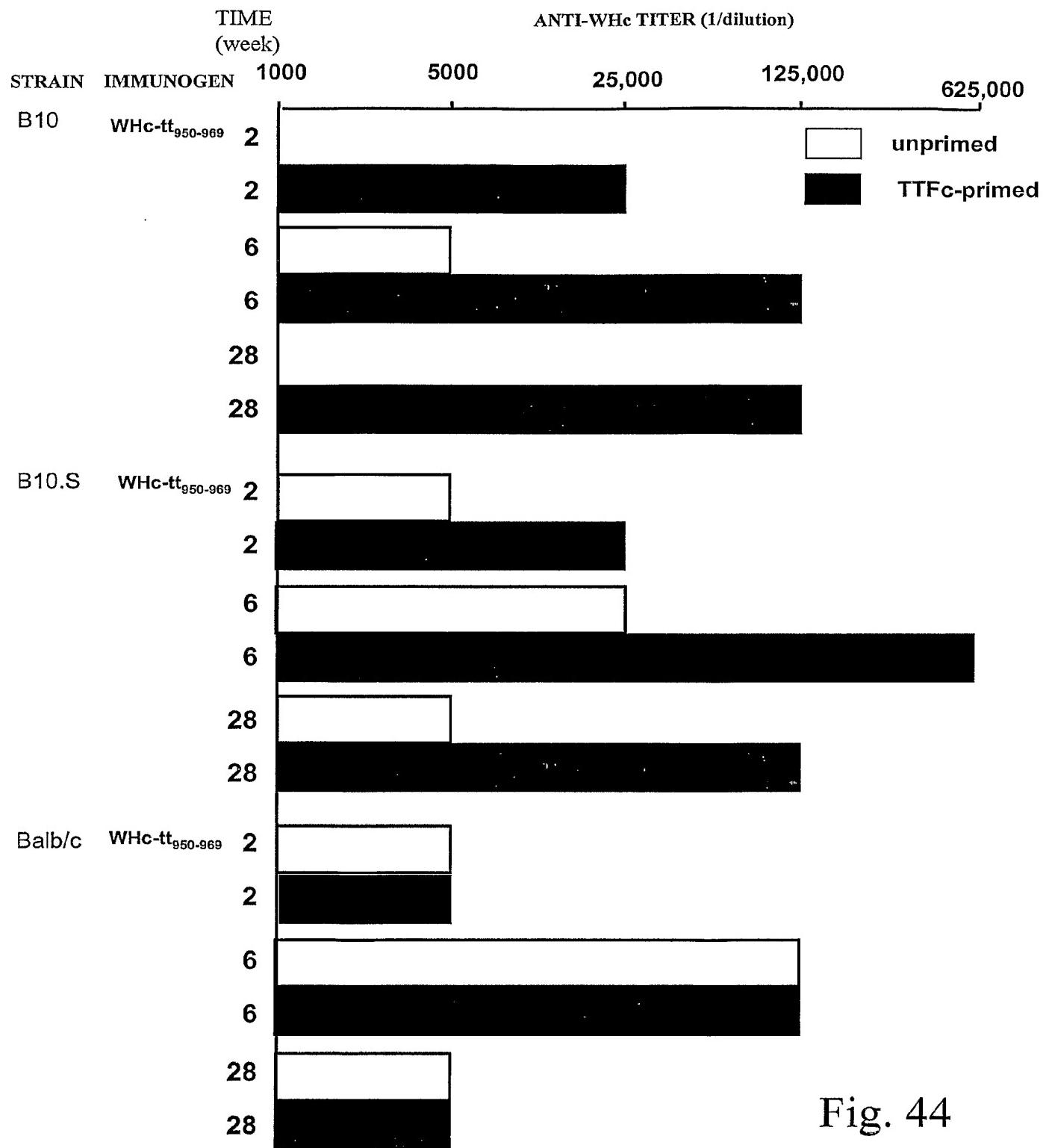


Fig. 44

Fig. 45

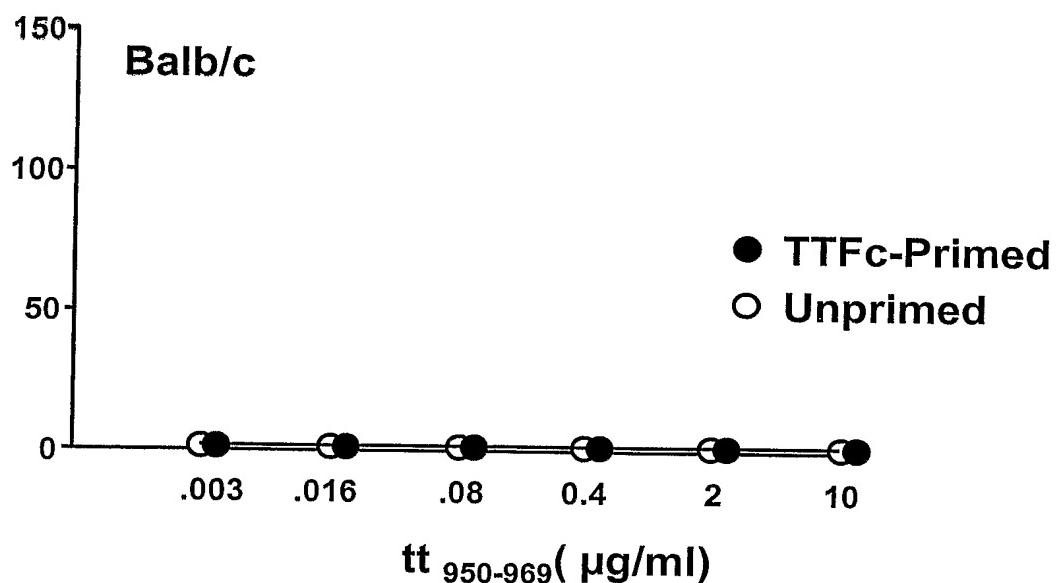
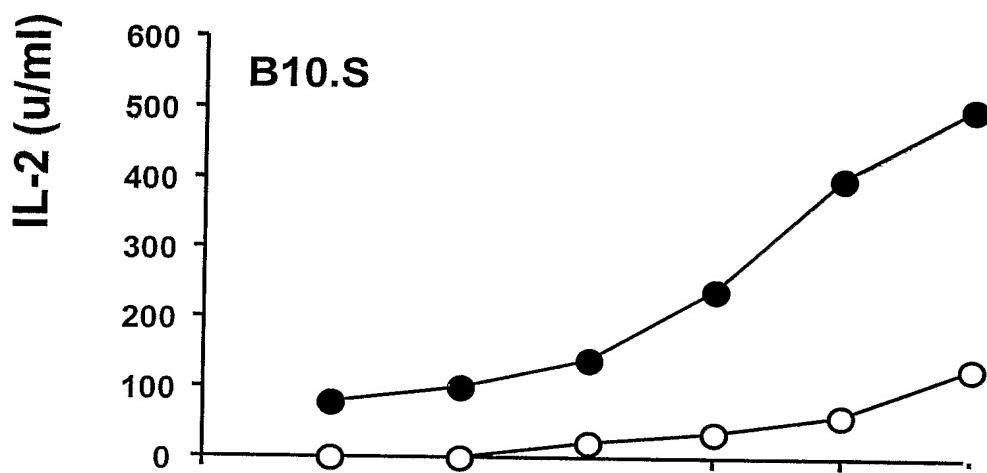
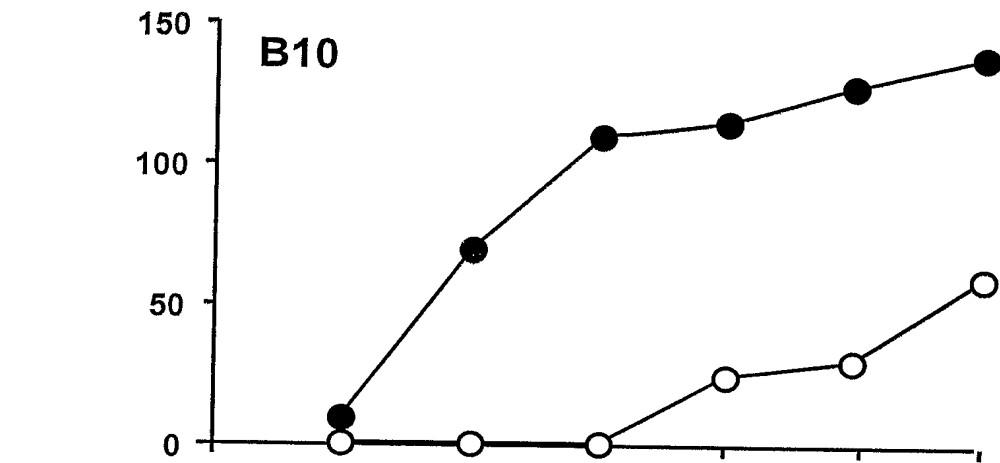


FIG. 46A

SEQUENCE ALIGNMENT

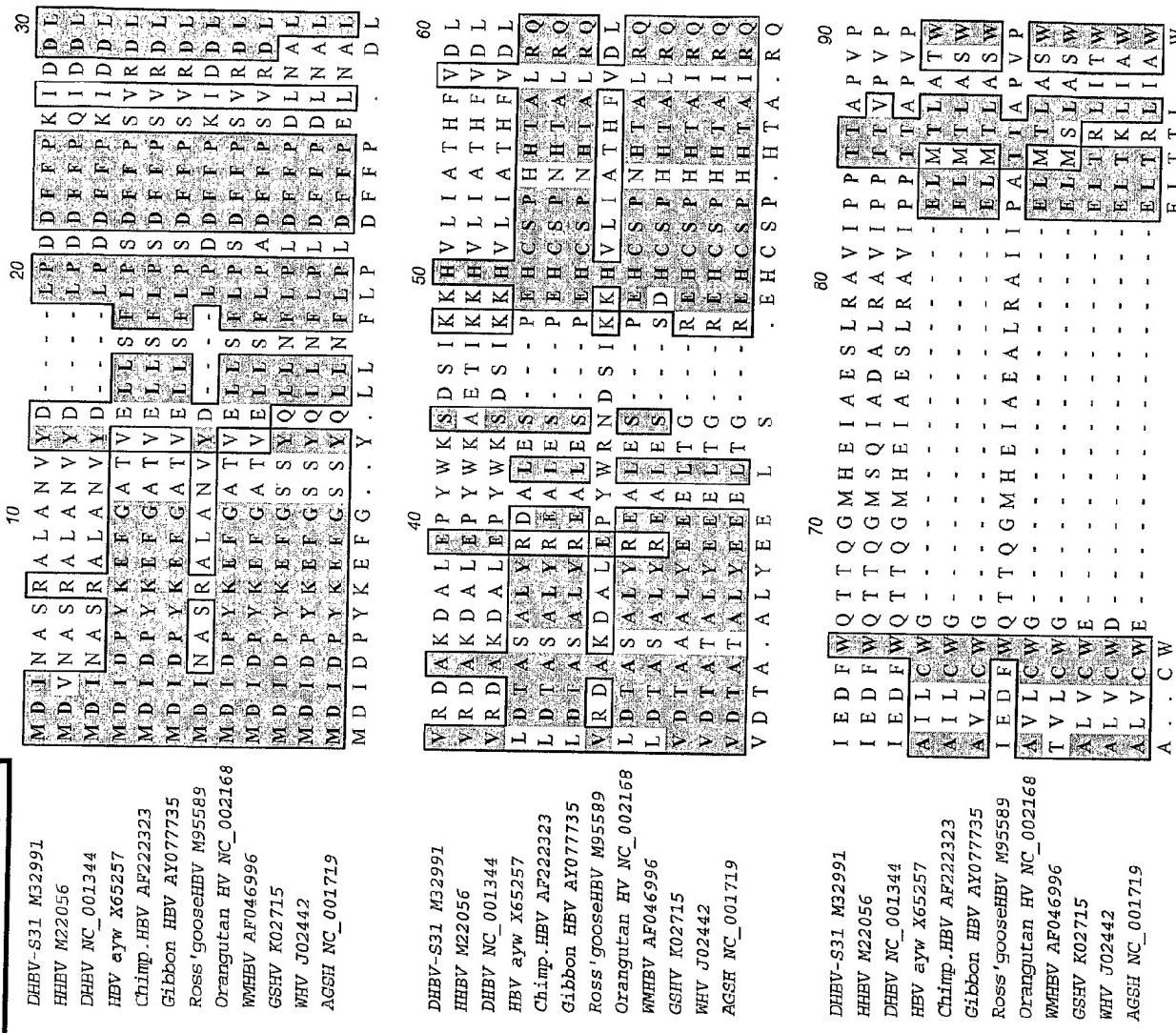


FIG.
46B

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HBBV M22056	E G F L I T H S E A E E I P L N D L F S N Q E E R I V N F Q
DHBV NC_001344	T G Y L I Q H E E A E E I P L G D L F K H Q E E R I V S F Q
HBV ayw X65257	V G V N L E D P A S R D L - - - - - - - - - - - - - - -
Chimp.HBV AF222323	V G N N L E D P A S R E Q - - - - - - - - - - - - - - -
Gibbon HBV AY077735	V G N N L E D P A S R E L - - - - - - - - - - - - - - -
Ross'gooseHBV M95589	Q G F L V Q H E E A E E I P L G E L F R Y Q E E R L T N F Q
Orangutan HV NC_002168	V G N N L E D P A S R E L - - - - - - - - - - - - - - -
WMHBV AF046996	V G T N L E D P A A R E L - - - - - - - - - - - - - - -
GSHV K02715	M S E N T T E E V R R I - - - - - - - - - - - - - - -
WHV J02442	M S S N I T S E Q V R T I - - - - - - - - - - - - - - -
AGSH NC_001719	M S A N I N S E E V R R V - - - - - - - - - - - - - - -
	G N . . . R E .
DHBV-S31 M32991	P D Y P I T A R I H A H L K A Y A K I N E E S L D R A R R I
HBBV M22056	P D Y P I T A R I H T H L R V Y T K L N E Q A L D K A R R I
DHBV NC_001344	P D Y P I T A R I H A H L K A Y A K I N E E S L D R A R R I
HBV ayw X65257	V V S Y V N T N M G I K E R Q I
Chimp.HBV AF222323	V V N Y V N T N M G I K E R Q I
Gibbon HBV AY077735	V V S Y V N N N M G I K I R Q I
Ross'gooseHBV M95589	P D Y P V T A R I H A H L K A Y A K I N E E S L D R A R R I
Orangutan HV NC_002168	V V N Y V N N N M G I K I R Q I
WMHBV AF046996	V V S Y V N D N M G I K V R Q E
GSHV K02715	I V D H V N N T W G I K V R Q I
WHV J02442	I V N H V N D T W G I K V R Q S
AGSH NC_001719	I V A H V N D T W G I K V R Q N
	V . . V N . . G L K . R Q L
DHBV-S31 M32991	T W W H Y N C E L W G E A N Y T N Y I S R L R T W L S T P E
HBBV M22056	L W W H Y N C E L W G E A N Y T N Y I S R L R T W L S T P E
DHBV NC_001344	L W F H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
HBV ayw X65257	L W F H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
Chimp.HBV AF222323	L W E H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
Gibbon HBV AY077735	L W E H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
Ross'gooseHBV M95589	I W W H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
Orangutan HV NC_002168	I W F H I S C L I T F G R E T V I Y I V S F G V V W I R T P P
WMHBV AF046996	I W F H I S C L I T F G Q H T V Q E F L V S F G V V W I R T P A
GSHV K02715	I W F H I S C L I T F G Q H T V Q E F L V S F G V V W I R T P A
WHV J02442	I W F H I S C L I T F G Q H T V Q E F L V S F G V V W I R T P A
AGSH NC_001719	I W F H I S C L I T F G Q H T V Q E F L V S F G V V W I R T P A
	L W F H . S C L T F G . T V E Y L V S F G V V W I R T P

DHBV-S31 M32991	K Y R G R D A P T I E A I T R P I Q Y A Q G G R K T S S G T	200
HHBV M22056	K Y R G K D A P T I E A I T R P I Q Y A Q G G R N Q T K G T	
DHBV NC_001344	K Y R G R D A P T I E A I T R P I Q Y A Q G G R K T S S G T	
HBV ayw X65257	A Y R P P N A P I I S T L P E T T V Y R R F G - - - -	
Chimp. HBV AF222323	A Y R P P N A P I I S T L P E T T V V R R F G - - - -	
Gibbon HBV AY077735	A Y R P P N A P I I S T L P E T T V V R R F G - - - -	
Ross'gooseHBV M95589	K Y R G K D A P T I E A I T R P I Q V A Q G G R N K T Q G V	
Orangutan HV NC_002168	A Y R P P N A P I I S T L P E T T V V R R F G - - - -	
WHHBV AF046996	A Y R P P N A P I I S T L P E T T V V R R F G - - - -	
GSHV K02715	P Y R P P N A P I I S T L P E H I V I R R F G G - S R A A	
W HV J02442	P Y R P P N A P I I S T L P E H I V I R R F G G - A R A S	
AGSH NC_001719	P Y R P P N A P I I S T L P E H I V I R R F G S - A R V V	
	Y R P P N A P I I S T L P E T V V R R F G - - - -	
DHBV-S31 M32991	R K P R G L E P R R R K V K T T F V Y G R R R S K S R E R R	220
HHBV M22056	R K P R G L E P R R R K V K T T V V G R R S K S R G R R	
DHBV NC_001344	R K P R G L E P R R R K V K T T V V G R R S K S R E R R	
HBV ayw X65257	R S P R R R T P S P R - - - - R R R S Q S P R R R	
Chimp. HBV AF222323	R S P R R R T P S P R - - - - R R R S Q S P R R R	
Gibbon HBV AY077735	R S P R R R T P S P R - - - - R R R S Q S P R R R	
Ross'gooseHBV M95589	R K S R G L E P R R R R V K T T V Y G R R R S K S R E R R	
Orangutan HV NC_002168	R S P R R R R T P S P R - - - - R R R S Q S P R R R	
WHHBV AF046996	R P S G R R R T P S P R - - - - R R R S Q S P R R R	
GSHV K02715	R S P R R R T P S P R - - - - R R R S Q S P R R R	
W HV J02442	R S P R R R T P S P R - - - - R R R S Q S P R R R	
AGSH NC_001719	R S P R R R R T P S P R - - - - R R R S Q S P R R R	
	R R R S Q S P R R R - - - - R R R S Q S P R R R	
DHBV-S31 M32991	A P S P Q R A G S P L P R S S S H H R S P S P R K	240
HHBV M22056	S S P S Q R A G S P L P R N R G N Q T R S P S P R E	
DHBV NC_001344	A P S P Q R A G S P L P R S S S H H R S P S P R K	
HBV ayw X65257	R - - - - S Q S R E S Q C	
Chimp. HBV AF222323	R - - - - S Q S P A S Q C	
Gibbon HBV AY077735	R - - - - S Q S P A S Q C	
Ross'gooseHBV M95589	A P T P Q R A G S P L P R T S R D H H R S P S P R E	
Orangutan HV NC_002168	R - - - - S Q S P A S Q C	
WHHBV AF046996	R - - - - S Q S P A S S C	
GSHV K02715	R - - - - S Q S P A S N C	
W HV J02442	R - - - - S Q S P S A N C	
AGSH NC_001719	R - - - - P Q S P A S N C	
	S Q S P P . S . C	

FIG. 46C